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SPECIALISM IN THE GENERAL HOSPITAL.*

By Sir William Osler, Bart.,

Regius Professor of Medicine, Oxford; Honorary Professor of Medicine, The Johns Hopkins University.

It is not easy to put in words my appreciation of the honor of delivering one of the formal addresses at the opening of this institute or to express my gratification at the inauguration of this new development in the Johns Hopkins Medical School. The pleasure is heightened by the thought that the generosity of an old and valued friend has made today possible. This hospital has already experienced the wise liberality of Mr. Henry Phipps, one of whose tuberculosis foundations, under its management, ranks as a model of its kind.

That, after nearly a quarter of a century, all those professionally concerned in the early working of the hospital are here to take part in this ceremony, is, for us at least, a happy circumstance. One man I should like to have seen with us, Francis T. King, the first president of the hospital, whose devotion to its interest and whose faith in its future were the stay and support of his declining years. Three of those closely connected with the early organization have passed away. Dr. John S. Billings was, from the first, the adviser of the board of trustees, the real designer of the hospital, and the friend to whom we all turned for advice. I know with what satisfaction he looked back on this part of a life great in achievements for the public and the profession.

No one of all that fine band of men with whom we were associated, Judge Dobbin, Judge Gwinn, Mr. Francis White, Mr. Lewis Hopkins, Mr. W. T. Dixon, Mr. G. W. Corner, Dr. Cary Thomas, Dr. Alan Smith, Judge Brown, Mr. James Cary, Mr. Joseph Elliott, Mr. C. Morton Stewart, would have appreciated to-day more keenly than Daniel C. Gilman, whose work in connection with the opening of the hospital must never be forgotten. He was a man with rare vision and one also who could drive the straight furrow, as the people of this state—of the country at large—well know. And how Isabel Hampton would have rejoiced to see this day—with its great opportunity to develop the special work so dear to her heart. How full of gratitude must be our first director, Dr. Hurd, to see the fruition of many years of strenuous, hopeful toil!

In 1889 this institution seemed to many the last word in hospital construction, and those of us who were fortunate enough to take charge of the departments felt that here was something to be lived up to, something in which our dreams could be realized. Only when in working order did we feel its incompleteness. We had no medical school, a big gap quickly filled by the generosity of Miss Garrett and her friends. Year by year saw new departments added, new lecture rooms, operating rooms, laboratories, additions to the out-patient de-

* Remarks made at the opening of the Henry Phipps Psychiatric Clinic of The Johns Hopkins Hospital, April 16, 1913.

partments, to the Nurses' Home, and, by Mr. Marburg to the private wards; and hand in hand, an internal growth in efficiency, and an ever-widening sphere of influence, educational and philanthropic. Our ambition was to do for medicine what Mr. Gilman and his faculties of the university were doing in arts and science, and at a pace hard to follow. The race was not an easy one, but fortunately there were close bonds between the two training stables, and we had the advantage of the prestige of their 13 years of brilliant success.

Only a few impressions of life endure. We use the same cylinders over and over again, the dots and markings become confused, and when we call for a record, a jumbled medley is poured out, a confused message from the past. But certain records are time-fast, and bite in such a way that no subsequent impressions can blur the clearness, and the story comes out fresh and sharp. So it is when I call up those early years so full of happiness, so full of hope. And to have seen in so many ways the fulfillment of our heart's desire is more than we could have expected, more indeed than we deserved.

I am sorry for you young men of this generation. You will do great things, you will have great victories, and, standing on your shoulders you will see far, but you can never have our sensations. To have lived through a revolution, to have seen a new birth of science, a new dispensation of health, reorganized medical schools, remodeled hospitals, a new outlook for humanity, is not given to every generation.

By temperament a dreamer, wherever I have worked, visions of the future have beset me, sometimes to my comfort, more often to my despair. In desolate days I have wandered with Don Quixote, tilting at windmills; in happier ones I have had the rare good fortune to dream dreams through the gate of horn, and to see their realization, to have both the vision from Pisgah and the crossing of Jordan. I have seen the school at which I began in Toronto, in an old building, dirty beyond belief, transformed into one of the most flourishing on the continent, a staff of seven teachers increased sevenfold; my alma mater, McGill, prosperous even then in men of mettle, but housed in wretched quarters, now in palatial buildings, and in affiliation with two of the best equipped of modern hospitals. How paltry were my aspirations of those days! How insignificant do they seem. My feelings when Sir Donald Smith, now Lord Strathcona, gave us the first endowment of $50,000, could not be stirred to the same intensity to-day by less than a million! Nearly 30 years have passed since I joined the University of Pennsylvania, the premier school of the country. There were new buildings, and a new hospital grouped about a single arts building. But what a transformation since! Whole squares of West Philadelphia annexed and covered with laboratories, dormitories and lecture halls and largely due to the magic energy of a prince of dreamers, William Pepper.

It has been my lot to see others do what I should have liked to do myself, and to feel that it has been better done! Looking back over a somewhat vagrant career, my fission from an academic body has always been a stimulus, and has invariably quickened the pace of progress. And this thought was a consolation when I left this comfortable billet, a few years ago. Among the scanty seeds scattered in my peaceful valedictory only those in which I ventured into the dangerous region of prophecy appear to have fallen on good ground.

I spoke of the needs of special departments—hoping that within 25 years we should have a psychiatric institute, a children's hospital, a genito-urinary clinic and a special building for diseases of the eye, ear and throat. Two of these are already accomplished facts—the Harriet Lane Johnston Children's Department, has been opened; to-day we open the Phipps Psychiatric Institute, and for the new genito-urinary clinic, that money has been furnished through the liberality of Mr. James Buchanan Brady. Others will follow rapidly, and it is safe to say that within a dozen years there will be as many special departments, semi-independent units in a great organization. The occasion seems fitted for the expression of a few thoughts on specialism in the general hospital.

The work of the units is identical; each a place where rich and poor receive the best skilled help that the profession can command; each a place where students are taught; each a center of study and research. Let us consider briefly these three functions. Similar in diversity, each unit in organization, in aims, and in methods, is a replica of the other. Each represents a technical school linked to the university by the medical faculty of which, by Mr. Hopkins' will, this hospital was to form a part. They differ from the more purely scientific departments of the medical school in one important particular. The hospital units mint, for current use in the community, the gold wrought by the miners of science. This is their first function.

A mother to-day brings her child to Dr. Harry Thomas, at the neurological department, a poor dwarfed, idiotic creature, but all the same very dear to her heart. It is a far cry from the little laboratory where Schiff made his immortal experiments, and literally thousands of workers in the mines of science have slaved years to find the pure gold, handed out freely from this hospital to that poor woman, with which salvation was wrought for her poor child. It seems so easy now. "Ah, a cretin. How interesting! How old do you say? Eight? Why, she looks three. All right, do not worry, the child will get well quick; get these powders. Yes, three times a day!"

An anxious mother, whose son goes to Manila next week, brings him to Dr. Barker in the private ward for an antityphoid inoculation. Again a far cry from Zurich, where Klebs—so often a pioneer—first saw the typhoid bacillus. Again, a host of miners and a vast store of gold—golden knowledge, with which, would they but use it, people of the country could redeem from certain death thousands of their sons and daughters.

The two incidents I have mentioned illustrate what is going on in every unit of a hospital today. Take another—that street brawl last night. "Yes, he was shot through the abdomen." "A dozen wounds in the bowls, you say? Hum! What a job! Must have taken you a long time—doing well,

of course." "Oh, yes, we got him early—they all do well now!" Who would have believed such a story in my student days? Again, the pure gold dug out by the elder Gross, Lister, Halsted and thousands of miners, minted in the laboratories and handed out, Mr. President, to the public last night by your surgeons.

We sit over the fire in the evening and pile on the coal without a thought of the dark and dangerous lives of the poor miners who risk so much for so little. It distresses my soul to think that we have done so little for the miners of science, and it does not lessen my distress to know that very often they do not give a thought to us. That coal put on the grate last evening—do you think the Hungarian in West Virginia thought how comfortable you would be over the fire? No! Nor did Schiff realize that his work would be utilized to brighten the hopes of thousands of mothers or that he was following a lode richer for humanity than the Golden Fleece. Only a cold-hearted, apathetic, phlegmatic, batrachian, white-livered generation, with blood congealed in the cold storage of commercialism, could not recognize the enormous debt which we owe to these self-sacrificing miners of science; and yet there are to-day sons of Belial, brothers of Schimei, daughters of Jezebel, direct descendants of the Scribes, Pharisees and hypocrites in the time of Christ, who malign these prophets and wise men, winners in a fight for humanity unparalleled in the annals of the race.

The perfect physical form in man or woman is much more sought than found. The perfect mental form is even more rare. The best to hope for in the average man, from nature and nurture, is to have a right judgment in all things. In how few of us is this consummation reached! One philosopher made the comforting remark that "Every man has a sane spot somewhere." Burton, in his survey of humanity in the famous *Anatomy of Melancholy* concludes that the whole world is mad, and needs a journey to Anticyra, (where the best hellebore, a specific against madness, was grown).

There should be, Mr. President, no lack of candidates for help from the unit we open to-day. Many a man goes to his physician now for an overhauling of his machinery. I found a big West Virginian in the private ward one morning. The history was colorless. I went over him thoroughly. "There is nothing the matter with you," I said. "I did not say there was," came the reply, "that is what I wanted to know."

We are all a bit sensitive on the subject of our mental health, but a yearly stocktaking of psychic and moral states, under the skilled supervision of Professor Meyer, would be most helpful to most of us.

Mr. J. A tendency to irritability of temper.

Mrs. R. Too much given to introspection.

Miss B. Over-anxious about her soul.

Master G. Worried by a neurasthenic mother.

These would be some of the headings in the diagnosis slips. But the Institute will have enough to do—meeting a demand for the early treatment of borderland and acute cases.

The progress in the rational treatment of insanity is a bright chapter in the history of the past century. The story recently told by Dr. Hurd, of the changes in this country within forty years, is full of encouragement. The larger staff, the skilled assistants, the scientific study of the cases has become a rule and this community has had the benefit of the up-to-date methods of the Sheppard-Pratt Hospital, and has seen with pride the rapid development of the work of the state institutions. New methods of treatment will be tested, every advance in technique controlled, and to new theories will be applied the touchstone of science. A wide diffusion of its benefits should take place through the nurses who will pass through the institute. The discreet, even-balanced, thoroughly trained mental nurse will be a great boon in general practice, and she will have a sociological value amid the widespread activities that have been aroused in connection with mental hygiene.

That the medical student is an essential factor in the life of a great general hospital, has been of slow recognition in this country. Admitted to the dispensaries, welcomed in the amphitheater, he has been, until recently, rigidly excluded from the wards, except as a casual attendant on ward classes. I am glad to say that from the day he leaves the medical school laboratories, he is in this hospital a co-worker with doctors and nurses, in every one of its activities, and as his right, not as a privilege grudgingly granted by the trustees.

And so it should be in all general hospitals. Every unit must be so organized as to make him fit in as part of its machinery. It is his business to know disease, and for the sake of the public, every possible opportunity should be given to him. I would even throw open the private wards, that the clinical clerks and surgical dressers might see the vagaries of sick life in all classes of society. In the palmy days of Rome, the physician was followed to the houses of the wealthy by his pupils—a practice we could emulate in our private wards—limiting, of course, the numbers, and selecting the cases.

But with the medical student there is a real difficulty, expressed 25 centuries ago by the Father of Medicine, in the famous aphorism "Life is short; the art is long". The stay of the medical student in the hospital is so brief, the amount to be learned so vast, that we can only hope to give him two things—method (technique) and such elementary knowledge as how to examine patients, the life history of a few great diseases and the great principles of surgical practice. He cannot be expected in the short period of the curriculum to go the circle of the units, spending time enough in each to master the chief details of a dozen specialties.

In most schools, a system of elective studies has been arranged to meet this really pressing and serious condition, which has grown in acuteness with the multiplication of the specialties? How can an institute like this touch the medical curriculum? At many points, directly and indirectly. The very existence in a general hospital indicates the recognition of psychiatry as part of its legitimate work. One of the tragedies of the subject has been a dissociation from centers of active professional and university life. A department of medi-

cine, with the closest affiliation with the life of the community, has been segregated and stamped with a taboo of a peculiarly offensive character. Here it will take its proper place—a unit in the work of the medical school of a university.

This, in itself, will be a lesson to the student. A new atmosphere will be diffused, a new group of energies and activities will come into the hospital, which cannot but be helpful. The director, his staff, and the nurses will play a new rôle, which will greatly enhance the reputation of the old company. Living as he does in such close fellowship with the staff of the hospital, the medical student will be influenced in this way by the very presence of the institute.

It is to be hoped too, time may be found for general instruction of the senior class in the elements of neuro-psychology, and with the elective system, an active group of students be found to whom this study will appeal strongly. But after all as practical men, we have to face the Hippocratic aphorism—the art is getting longer and longer, the brain of the medical student, not getting bigger and bigger, has its limits; and though keener and more industrious than ever in history, the time is too short for a man already burdened to the breaking point, to study any specialty from the standpoint of the specialist.

To a large outside body, this institute should cater with extraordinary benefit. There must be a thousand or more assistants in the asylums of the country, whose pineal glands are not yet crystallized, and who should find here inspiration and help. Amid isolated and depressing surroundings, these men do yeoman work in the profession. From the director and his staff, they will receive that warm and encouraging sympathy, the very leaven of life, a quality which has been the inspiration of the benefactions of the founder of this institute. And I hope room and plenty of it will be found for the general practitioner, through whom more than any other group, the benefits of this institute may be distributed. He needs enlightenment, instruction and encouragement—enlightenment as to the vast importance of early deviations from normal mental states, instruction in new methods of diagnosis, and treatment and encouragement to feel that in the great fight for sanity in the community he is the man behind the guns.

A larger outlook is connected with the third function of a hospital unit. The old Greek, with his quick sense of helpfulness, always asked about a work: "Does it make life a better thing?" and Prof. Gilbert Murray remarks that one who wished to give the greatest praise to the Athenians said, "They strove to make gentle the life of the world." The American, the modern Greek—mentally if not orally—always asks the same practical question; sometimes, in the case of pure science, when it is both foolish and fruitless. But he may ask legitimately how such an institute as this may be helpful in studying lapses and freaks of the human mind—I cannot give the answer. "It is not in the book I learned out of" as the children say. I could tell you in internal medicine, and could refer you to the long list of studies in dysentery, malaria, typhoid fever, pneumonia, heart diseases and blood diseases that have come from the medical unit. But a psycopathic unit is a novelty in a general hospital, designed for the study as well as for the cure of mental aberrations.

We talk a great deal about the human mind, and, when cornered, quote Hamlet to cover an unpleasant ignorance of its true nature. The modern student, like the ancient, takes his stand either with Plato and compares the mind and brain to a player with his musical instrument, or with Lucretius to a musical box wound up for so many years to play so many tunes. Authorities lean to one or other of these views, and I have a shrewd suspicion that some of our distinguished visitors, great representatives in this specialty, do not see eye to eye in this matter. Three things we do know, departures from normal states are extraordinarily common—they are the most distressing of all human ills—they should be studied systematically by experts, with a view to their prevention and cure.

When Dean Swift left the little wealth he had to found a house for fools and mad, he could not forego the pleasure of adding the satiric touch: "No nation needed it so much." This idea, was not, I am sure, in the large heart of Mr. Phipps; but a wide-spread feeling has arisen in this country that the hygiene of the mind is just as important as the hygiene of the body—that we must return to the Greek ideal of the fair mind in the fair body. How beautifully Plato visualizes the day (in a passage I am never tired of quoting)—"When our youth will dwell in a land of health amid fair sights and sounds and receive good in everything; and beauty, the effluence of fair works, shall flow into the eye and ear like a health-giving breeze from a purer region, and insensibly draw the soul from earliest years into likeness and sympathy with the beauty of reason." (Republic, Bk. II.)

What a revelation of an awakening in the community that it was possible to organize such a Congress of Mental Hygiene as was held here a few months ago under the auspices of the Medical-Chirurgical Faculty! The program itself was an inspiration. In this country, to recognize a wide-spread need is to meet it; and such gatherings held under auspices of the National Committee will go far to lessen the sad prevalence of early nervous breakdown.

What a philosopher said of the Melissians may be said of many people—they are not fools, but they do just the things that fools do, in the matter of training the young. Unfortunately, we cannot pick our parents, and still, as of old, our hearts give our hands, regardless of our heads. Dr. Mott will tell a tragic tale of heredity in relation to insanity. I am afraid several generations must pass before we see any practical results of the present active eugenic crusade, but there is an immense and hopeful work to be done in educating parents in training-stable methods. An Ethiopian cannot change his skin, but a queen bee results from a change of diet. This institute, I am sure, will play its part in this national campaign of prevention of mental ill health through education—a campaign as important to the public, and just as

worthy of support as the great struggles against tuberculosis and infant mortality.

It will be helpful too, to study in a sane, sober and sympathetic way, epidemics of mental, moral and even economic folly as they sweep over the country. The present opportunity should not be missed. With causes just as definite as smallpox or yellow-fever, they never occur under exactly the same conditions, but all have their basis in, and are mere specks upon, that fine old humanity that is ever fighting its way towards the light.

The present out-break has not been equaled since the capture of the Roman world by Oriental cults. The same old-fashioned credulity exists that enabled Mithras and Isis, Apolonius and Alexander to flourish then as the new cults do to-day—and for the same good reason. There is still potency in the protoplasm out of which arose in primitive man, magic, religion and medicine. Circe and Asculapius were probably twins! Historically our fringe of civilization is of yesterday, if we compare the six or seven thousand years of its record with the millions which must have passed since man assumed his present form on the earth. In this vast perspective Aristotle and Darwin are fellow-students; Hippocrates and Virchow are contemporaries.

Primitive views still prevail everywhere of man's relation to the world and to the uncharted region about him. So recent is the control of the forces of nature that even in the most civilized countries man has not yet adjusted himself to the new conditions, and stands, only half awake, rubbing his eyes, outside of Eden. Still in the thaumaturgic state of mental development, ninety-nine per cent of our fellow creatures, when in trouble, sorrow or sickness, trust to charms, incantations and to the saints. Many a shrine has more followers than Pasteur; many a saint more believers than Lister. Less than 20 years have passed since the last witch was burned in the British Isles!

Mentally the race is still in leading strings, and it has only been in the last brief epoch of its history that Esop and Lewis Carroll have spun yarns for its delight, and Lucian and Voltaire have chastized its follies. In the childhood of the world we cannot expect people yet to put away childish things. These, Mr. President, are some of the hopes which fill our hearts as we think of the future of this new department.

One word of appeal to the units. Members of a corporate body, successful life will depend upon the permeation by harmonics which correlate and control the functions. Isolation means organic inadequacy—each must work in sympathy and in union with the other and all for the benefit of the community—all toward what Bacon calls the lawful goal of the sciences, that human life be endowed with new discoveries and power.

SOME MODERN PROBLEMS IN NUTRITION.*

By Dr. Franz Knoop,

Professor of Physiological Chemistry, University of Freiburg, Germany.

Physiological chemistry is concerned with the chemical rearrangements which are constantly in progress in all living organisms. The continuity of these transformations is possibly the most striking characteristic of what we term "life."

Physiological chemistry finds its greatest support from the uses which practical medicine makes of its results, and thus to a large extent it has dedicated itself to the task of elucidating all the chemical changes occurring in the human organism. The most direct way to attack this extraordinarily complicated problem as a whole, is to make a comparison of the chemical composition of the organism's intake and output. Physiology has devoted itself, at enormous expense, to investigations aiming at the attainment of an exact metabolic balance. This method of investigation furnished chiefly quantitative results, for qualitatively, it concerned itself with substances which, from a chemical point of view, were exceedingly ill-defined. By degrees, this drawback has been in part removed. For example, the main facts, concerning the chemistry of the proteins have only been recognized during the present century.

Cellular material from plants and animals, especially mammals, constitutes the main source of our food substances. Hence the study of these food substances is closely allied to the chemical analysis of the human body, for the latter, considered from the standpoint of chemical classification, does not differ essentially from the animal food which supports it.

These descriptive studies, which we may regard as a sort of chemical anatomy of the human body, are essential for the intelligent investigation of the chemical functions of the body. They are the more important, since the food substances of the body are not utilized as is the fuel of an engine, whose parts are independent of its source of energy. In the animal organism, the food units have actually to furnish the ever-changing parts of the machine consuming them. The constant regeneration of these parts constitutes an important part of their chemical functions.

Anatomy and physiology are seldom so intimately united, as when function and composition of cell aggregates are considered from a chemical standpoint. It is surely a sign of a lack of understanding when descriptive chemical studies of this character are regarded by physicians as purely chemical, simply because their biological significance is not obvious at the present time. It is true that pure chemists, without any biological interests, may take up work of this character and, indeed, they have done so in many lines of investigation. But

* Paper read at a meeting of The Johns Hopkins Hospital Medical Society, March 17, 1913.

often this has not been done, and then it is left for biology to till the ground, which may yield a harvest to succeeding generations only.

Metabolic physiology, using the term in the old sense, knew but little of the detailed structure of the food substances. It concerned itself with the needs of the entire organism under the most varying conditions, with the availability, thermodynamic effect, value and utilization of the individual food-substances for various purposes. The experimental conditions were varied to include work and rest, hunger and satiety, fœtal life, youth and old age, fever, subnormal temperatures and hibernation, the effects of high altitudes and sea-level, and so on. Valuable information was gathered in this way, but progress beyond a certain point was impossible, and from a purely chemical point of view, such studies were not particularly fruitful, for nothing definite was known as to what substances were qualitatively essential to the organism. Thus, meat which has been extracted with ether is lacking in a certain substance which cannot be replaced by the definitely characterized chemical substances of the ether-extract, and the experimental animal, fed with such extracted material, ceases to thrive. Feeding exclusively with polished rice leads to a fatal condition with the development of symptoms similar to beri-beri. These symptoms may be quickly and completely abolished by the administration of about one milligram of a substance contained in that part of the rice which has been discarded. This substance belongs to none of the known groups of food-substances. What is it? Is it always necessary, or only in conjunction with a rice diet? We do not know. In questions of this nature, we feel our ignorance on every hand.

The methods of metabolic physiology in which only the gross effect is considered, can help us but little in obtaining an insight into these chemical changes, the elucidation of which promises an altogether deeper insight into the varied types of vital processes. The recent development of biochemistry has clearly shown, that we stand only at the threshold of such new points of view. Historically, how much better off morphology appeared, which, having at its disposal highly developed optical methods of investigation, gave such an overwhelming stimulus to the tendency to consider all the problems of natural science from a descriptive point of view, that, for a time, it was believed that the most important problems of function could be solved by the microscope. Even now, in the education of medical students, we find descriptive methods still predominating to an extent, which is only historically intelligible. Necessary as a knowledge of cellular structure is for the understanding of function, we must remember that, to quote the words of Hofmeister, the microscope shows us only the empty stage, the action on which is revealed to us only by totally different methods of research.

What is true for the individual cell is equally true for the whole body with its various organs. We are more and more struck by the fact that relations between different parts of the body are not exclusively controlled by visible morphological factors, and I need only mention the names adrenalin, and secretin, pituitrin and iodothyrine, to recall to your mind a series of organs about whose chemical functions we are partially informed, but about which anatomical investigation has taught us almost nothing. Starling introduced the conception of hormones for these carriers of chemical impulses, among which may be mentioned the body causing the proliferation of mammary tissue following the injection of fœtal extracts. Here, where the work of Jacques Loeb on the chemical stimulation of development is so well known, it is unnecessary to emphasize the prime importance of chemical studies with regard to processes which, in the past, have been relegated exclusively to morphological investigation.

The hormones which regulate the vital activities of the whole body, are produced by the organism itself, and the chemistry of the formation of these substances must be altogether distinct from the normal breakdown of food material. We can hardly hope to understand these special reactions until we have attained an adequate picture of the normal catabolism of the substances which primarily furnish energy to the organism. Metabolic physiology has had little to say concerning these matters. It has indicated the possibility of the mutual replacement and possible interconversion of some of the main groups of food-substances, and it has shown that the conversion of protein, fat and carbohydrate to carbon dioxide, water, urea and sulphuric acid does not always follow the most direct path. But knowledge as to how these reactions occur and how they may be modified, can only be obtained from a detailed chemical analysis of these intricate changes, and at present our methods are inadequate for the task. If we consider as our first and final quest the formulation of equations which shall indicate, step by step, the gradual conversion of food-substances into the end products of metabolism, we shall find much that is helpful and stimulating. Oxidation reactions in the living organism are characterized by their slowness and regularity and the constancy of such conditions as temperature, pressure, reaction, etc., constituting a mechanism that we can hardly hope to imitate. It is the unique and extraordinarily complete character of this mechanism of the living organism, that makes it so generally interesting a subject for investigation.

After metabolic physiology had been for some time in a state of stagnation, the new ideas leading from a chemical conception of the intermediate paths of catabolism, quickened the whole subject into renewed activity. Unsuccessful attempts had long been made to try to determine in the normal organism intermediate products, which would directly indicate the paths of normal metabolism. This is a most remarkable fact. We may perhaps understand this best if we assume that only a few molecules of a substance undergo oxidation simultaneously, and that their catabolism is complete before new molecules are attacked. Thus but few molecules will, at any one time, be in the first, second or third stages of oxidation, and the concentration of intermediate products of catabolism must always be low.

It was only when pathological or experimentally changed conditions were made use of, or isolated surviving organs were

employed, or the fate of foreign substances in the body was investigated that certain laws were developed, which subsequently proved to be applicable to the normal organism. Up to this time practically only hydrolytic changes, such as the breaking up of CO and CN groups with addition of water, had been observed. This type of change is seen in the conversion of protein into amino-acids with intermediate formation of albumoses and peptones, or in sugar production from starch, or fatty acids and glycerine from fats. But none of these reactions, which are effected by the digestive ferments, involve oxidation and they liberate no significant amount of energy and bring about no alteration in the chains of carbon atoms. The type of change involved in oxidation was first recognized in connection with the fatty acids, but even here, in spite of the fact that about 100 grams a day may be burned, it was impossible to isolate intermediate products directly. When, however, a group resistant to attack in the body was introduced into the fatty acid molecule, it became possible to detect intermediate products. For this purpose phenyl substituted fatty acids were employed, the homologues of which are found among the products of intestinal putrefaction and which are constantly being absorbed. By using these substances, it was possible to show that fatty acids undergo oxidation in such a way that the oxygen invariably attaches itself to the β-carbon atom and the ketonic acid thus formed yields, on further oxidation, a saturated fatty acid, containing two less carbon atoms.

Thus it has been possible to determine the chief path followed by the fatty acids in their breakdown and to recognize the intermediate products which we are likely to encounter. This conception has led to an intelligible understanding of the origin of the acetone bodies from fatty acids in the diabetic organism. Similarly, the fact that the fatty acids, present in milk-fat, all contain an even number of carbon atoms, may be explained on the supposition that they are derived from one another by a process of β-oxidation. Many other examples of the helpfulness of this hypothesis might be cited.

It is of interest to note, that the possibility of the above-mentioned physiological reaction was doubted by chemists, owing to the fact, that such a reaction had not been observed in the chemical laboratory. The frequent observation of reactions and mechanisms in the living organism, which have not been hitherto observed, is certainly one of the stimulating attractions of biological research. This is especially true with regard to biochemical questions, since chemistry, perhaps more than any other science, has occupied itself with reactions, occurring in the test-tube without regard to natural processes. In many cases it is left to bio-chemistry to first unravel these intricacies by the investigation of natural objects. However, in the particular case, with which we are concerned, Dakin was able to assist in its development and also to show that the hitherto unobserved reaction might be successfully imitated in vitro. This change was brought about by hydrogen peroxide, an agent whose action frequently closely resembles that of the animal oxidizing agents.

After a general scheme for the metabolism of fatty acids had been established, a successful attempt was made to gain an insight into the mechanism of the breakdown of the amino-acids derived from proteins. This was done by using essentially the same method which had been helpful in the case of the fatty acids; that is to say, by the use of phenyl substituted homologues. The protein *Bausteine* or units are largely made up of amino-acids, all of which contain their nitrogen similarly linked to the α-carbon atom. This nitrogen may be split off in the form of ammonia, leaving an α-ketonic acid containing the radical—CO-COOH. The CO group, whether in the α or β position, forms a *punctum minoris resistentiæ* for the attack of oxidizing agents. It follows, therefore, that one carbon atom is removed as the first stage in the oxidation of α-ketonic acids, while the β-ketonic acids derived from the fatty acids part with two carbon atoms. Thus the amino-acids are converted into fatty acids, and these nitrogen-free radicals from proteins behave as fatty acids in their subsequent transformations.

In the course of these investigations upon fatty and amino-acid catabolism, the behavior of a large number of hypothetical intermediate products, including ketonic and hydroxy acids, unsaturated acids and acids with branched chains, etc., has been investigated and many valuable details have been discovered. Of these, I shall only mention the reduction processes by which ketonic acids are converted into hydroxy acids, and even into fatty acids. For these results form the chemical basis for the comprehension of fat formation from sugar, a reaction which must clearly necessitate far reaching reductions. Similar reactions lead to the reduction of acetoacetic acid to β-hydroxybutyric acid, and we now believe, with Dakin and others, that acetoacetic acid is the primary product from which β-hydroxybutyric acid is formed by secondary reduction. Formerly, the change was believed to be in inverse order.

One effect of these numerous discoveries has been to establish firmly the capacity of the animal organism for bringing about endothermic reactions, and furthermore, they have paved the way to a revision of many traditional theories. A principle long held by Pflüge that carbohydrates could originate only from carbohydrate substances has had to be abandoned, as the result of numerous experiments, particularly upon diabetics. For now we know that other food substances, such as protein, may yield carbohydrate, and American investigators have determined quantitatively the formation of sugar from a number of protein *Bausteine*.

The possibility of the reverse change, namely, the formation of protein from sugar and ammonia, was apparently excluded, for the statement that the nitrogen requirement of mammals could only be furnished by protein-like substances, was regarded as one of the most firmly founded dogmas of the old metabolic physiology. But in connection with the foregoing question, I should like to show how valuable for metabolic physiology an exact inquiry into chemical detail may be.

Every animal, even when overfed, constantly excretes in

the urine a certain amount of nitrogen, which is derived from cell protein used up as the result of cellular functions. During starvation, this nitrogen minimum rapidly reaches a constant value, and, until recently, it was believed that this could not be influenced by inorganic nitrogen but only by protein. When it came to be recognized that protein underwent a far reaching hydrolysis in the intestine, with the production of amino acids, it was inferred and subsequently proved that these latter substances could maintain the nitrogen equilibrium, that is, the balancing of the nitrogen output in the urine by the nitrogen containing substances of the food.

The capacity for synthesizing protein *Bausteine* from inorganic nitrogen was ascribed solely to plants and amino acids seemed to be the simplest substances capable of meeting the nitrogen requirements of animals. As a result of our knowledge of the breakdown of the amino acids, we are now in a position to admit this question to a revision. May not the organism, after all, be able to utilize inorganic nitrogen, that is to say, the same ammonia liberated by the breakdown of amino acids according to the first catabolic reaction already referred to?

The ammonia must, first of all, be brought in contact with substances which are formed simultaneously with it in the organism, such as ketonic acids. These experiments were successful, for it was found that the animal body can synthesize amino acids from ammonia and ketonic acids, into which they may be reconverted later. The catabolic reaction is evidently reversible. We must therefore abandon the conception of differences between plant and animal chemistry, based upon the supposed inability of the animal body to effect syntheses. Ammonia is constantly present in small quantities in the animal body, and α-ketonic acids, which may react with it to give amino acids, originate, as we know, not from fatty acids, but from sugar. We know relatively little of the oxidative catabolism of sugar, but we do know that in one way or another, lactic acid and pyruvic acid may be formed, and that both of these may be combined with ammonia to form protein *Bausteine*, especially alanine.

We are now in a position to understand the protein sparing action of carbohydrates, while fatty acids yielding β-ketonic acids which are not convertible into protein *Bausteine*, have not the same action. Fact and theory agree. But now, if the reaction involving the liberation of ammonia from the amino acids is reversible, one would expect that the administration of ammonia would influence the synthesis and exert a protein sparing action. This theoretical deduction has been confirmed in a number of ways. Investigations by both clinicians and physiologists have shown that animals may be maintained almost in nitrogenous equilibrium for weeks at a time, with ammonia as their sole source of nitrogen. It would seem, therefore, as if the consumption of the protein material of the cells might be reduced almost to nothing, if only an excess of carbohydrates is administered.

I should like you to notice, how the exact investigation of this single chemical reaction and the demonstration of the short equation:

$$-CO-COOH+NH_3 \rightleftharpoons -CH\,NH_2\cdot COOH+O$$

together with other similar researches in intermediary metabolism has entirely revolutionized the teachings of the investigations of the laborious older metabolic physiology. No clearer proof could be offered of the value of exact chemical analysis in biological research.

Thus we see how products of intermediary metabolism may react with one another; for example, those from amino acids with those from sugar. Doubtless also substances derived from fat, protein and carbohydrates may combine with one another. It appears probable that the synthesis of fat, following excessive consumption of other forms of food, may find its explanation in a process of reversible fatty acid catabolism. Possibly acetaldehyde or acetic acid compounds derivable from all of the three chief groups of food substances, may undergo condensation with formation of unsaturated or oxy compounds. These, in turn, may undergo reduction with formation of fatty acids with their long chain of carbon atoms. This type of reduction has already been observed in the case of benzoylpropionic acid and the corresponding unsaturated acids.

Another example of such a reaction has been noticed in connection with the synthesis of amino acids in the animal body. It was found that an acetic acid radical may attach itself to the nitrogen group, but we are not yet fully informed as to the origin of this acetyl group. It will be noticed that this aliphatic group is combined in precisely the same fashion as are phenylacetic and benzoic acids combined with glycocoll in hippuric and phenaceturic acids. It would seem as if we were dealing with a reaction of general significance. Just as in the proteins the acid carboxyl groups are combined as acyl radicals with the basic amino groups, so we may picture the acid end products of fatty acid oxidation combining with amino acids. Possibly our experiences with aromatic substances containing the benzoyl and phenacetyl groups may be found true in the case of their aliphatic homologues.

Whether the acyl radicals originate from the decomposition of sugar, for example pyruvic acid, or whether they come from acetoacetic acid, is capable of experimental determination by observing whether the yield of such condensation products is increased on feeding with fat or with carbohydrate. Should the mother substance of these acetyl groups prove to be the acetone bodies, which, as we know, do so much injury in the stages of acidosis in diabetes, it is possible that the feeding of easily acetylated substances may prove of therapeutic value. Such substances, perhaps might take up considerable quantities of these acids in the form of acetyl groups and thus make them less harmful. Such a line of research should be of direct interest to the practitioner of medicine.

The more we succeed in unravelling the details of the chemical mechanisms of the animal body by tracing the individual reactions, the more likely are we to investigate successfully what we may call the bypaths of metabolism in which sub-

stances undergo reactions for other purposes than simply a liberation of energy. It is surprising to note how the smallest derangement of chemical conditions in the body may result in far reaching injury.

We have a fairly clear picture of the reactions by which the pharmacologically active adrenalin may be formed from tyrosine. The change necessitates the splitting off of carbon dioxide, methylation and the introduction of two hydroxyl groups. It has recently been shown that a number of substances contained in ergot which have long been used therapeutically, may be derived from different protein *Bausteine* by a similar reaction leading to the removal of carbon dioxide. The close chemical relation between food substances and most powerful poisons, is very striking. It is through reactions such as these, that toxins and other noxious bacterial products may be formed.

Almost all manifestations of disease have a chemical basis. But can we hope to comprehend these when we know so little of the normal chemical mechanisms of the organism? Every branch of medical science is calling chemistry to its aid—pathology, internal medicine, bacteriology and serology. Pediatrics has become largely a study of the chemical pathology of nutrition, and even in such subjects as diseases of women and nervous diseases, progress is sought by chemical methods. In the universities of the Old World, new branches of learning, anxious to throw off restraints, progress but slowly. They must develop, as a rule, from existing departments which, owing to their own limited resources, are often slow to lend a helping hand. Time is required to bring about the needed changes. In this country of unlimited possibilities, such restrictions need not be reckoned with and the favorable conditions we see here promise a development for our science that may soon rival that of Europe.

May our science and practical medicine flourish, and rising above all personal and national considerations, serve the great cause to which we are all devoted—the welfare of mankind.

THE WASSERMANN REACTION IN THE JOHNS HOPKINS HOSPITAL.

By RALPH H. MAJOR, M. D.,
Assistant Resident Physician.

(From the Medical Clinic, The Johns Hopkins Hospital.)

Since the application of the Bordet Gengou principle of complement fixation in the diagnosis of syphilis by Wassermann, Neisser, and Bruck, the vast number of reports from clinics all over the world have proved the great value of this method. The Wassermann Reaction has been extensively employed in The Johns Hopkins Hospital in the past four years, and our experience with it confirms the results of a host of workers as to its reliability and specificity as a diagnostic procedure. The first report upon its use in this clinic was made by Clough,[1] in 1910, and comprised observations extending throughout the year 1909. Since that time no report of the results in this clinic have been published. It was thought that perhaps a résumé of the more recent cases would prove of some interest, and at the suggestion of Professor Barker all the cases have been collected, upon which this reaction was done the past year, from September, 1911, to August, 1912.

The technique of this reaction is now so well known that a detailed description of it is quite unnecessary. In the main we adhere to the original technique described by Wassermann, Neisser, and Bruck, except that an alcoholic extract of fetal luetic liver instead of watery antigens, has been employed. While Wassermann,[2] as late as 1910, still maintained the superiority of watery extracts over alcoholic, yet Bruck [3] recommends alcoholic solutions as giving identical results. The greater stability of the alcoholic antigen is perhaps the strongest point in its favor, and has resulted in its supplanting, to a great measure, the watery antigens.

Following the discovery of Marie and Levaditi [4] and others, that extracts of normal guinea-pig's heart were able in the presence of syphilitic serum to fix complement, many workers began to use such extracts as antigen. Further work, however, by Wassermann,[5] Plaut,[6] and Bruck l.c. indicates that a specific antigen is superior to a non-specific one and gives a higher percentage of positive reactions in luetic cases. In this clinic the antigen employed is prepared from fetal syphilitic liver, which we have always been able to obtain and against which no worker has raised any objection. The liver is ground up, mixed with nine parts of absolute alcohol, shaken for twelve hours, allowed to remain in the thermostat at 37° C. for 48 hours, then filtered, and the clear filtrate used.

The patient's serum before using is inactivated at 56° C. for one-half hour, and anti-sheep rabbit serum plus sheep red corpuscles is employed as the hemolytic system. We have not had in this clinic any extensive experience with Noguchi's [7] modification of the Wassermann reaction, but feel that the work of Dean,[8] Bailey,[9] and others does not point to normal anti-sheep amboceptor as playing an important rôle in obscuring positive reactions.

As complement, fresh guinea-pig's serum diluted 1:10 is employed. The complement and amboceptor are titrated each time just before using—the *Vorprüfung*—and three or four times the titer of the amboceptor is employed for the final tests. The tubes are placed in a water bath at 37° C. for one-half hour to fix the complement, and then left in the bath for one hour to allow hemolysis to take place.

Since the introduction of the Wassermann reaction in this clinic, it has been employed as a diagnostic method in practically all cases giving a history at all suspicious of lues, and has also been used in a great many obscure cases where the diagnosis was in doubt.

During the past year, from September 1, 1911, to August 1, 1912, the Wassermann reaction has been performed upon the sera of 1200 patients, the great majority of whom were medical cases. This number includes a great variety of diseases ranging from outspoken cases of syphilis to neurasthenic patients, in whom the reaction was done for the purpose of excluding lues. This series includes a great variety of functional and organic nervous diseases, cardiac diseases, nephritis, diabetes, pneumonia, typhoid fever, gastro-intestinal diseases —in fact, almost every medical disease seen in an active clinic during the course of a year. A fairly large number of cases of brain tumor from Prof. Halsted's service have also been included.

Of these 1200 cases, 239, or 20 per cent, gave positive reactions; while 961, or 80 per cent, were negative. Of the cases giving positive reactions, 55, or 24 per cent (nearly one-fourth!), gave no history of a primary sore. The percentage of negroes in the above figures is of some interest. The Wassermann reaction was performed upon 185 negro patients, the great majority being cardiac or cardio-renal cases, but also including numerous other more uncommon diseases. Of this number, 61, or approximately 34 per cent, gave positive reactions; while 124, or 66 per cent, were negative. When this number is compared with the reactions on white patients, it is seen that 34 per cent of negroes compared with 17 per cent of whites, give a positive reaction. This indicates a frequency of positive reactions in negroes twice that of the whites. These figures do not perhaps give a sufficient indication of the greater frequency among negroes, since the total number of reactions performed on the sera of colored patients is considerably less than that on whites.

The results of the Wassermann reaction in certain diseases deserve separate comment.

Aortic Insufficiency.

The Wassermann reaction in 42 cases of aortic insufficiency showed 21, or 50 per cent, positive reactions; while 21 were negative. Of the 21 negative cases, all but six gave a history of rheumatic fever, four of the six showed marked arteriosclerosis, and one patient included in the six died of an acute aortic endocarditis.

The above figures include both aortic insufficiency alone and in association with other heart lesions. The cases of pure aortic insufficiency show different results. Of 14 cases of pure aortic insufficiency, 13 were positive and only one negative. This patient with the negative reaction showed, however, partial fixation and gave a history of a primary sore twenty years before. This shows that in our series of pure aortic insufficiency, 93 per cent gave positive reactions, more striking figures than those of Citron,[10] who found that in 13 cases, 62 per cent gave positive reactions. Donath[11] found 90 per cent positive in 10 cases of pure aortic insufficiency, Longcope[12] found 81 per cent positive in 18 cases, and Collins and Sachs[13] saw 92 per cent positive in 13 cases.

Aneurysm.

In this series the Wassermann reaction was applied in 22 cases of aneurysm, mostly of the aortic arch. Twenty-one, or 95 per cent, gave positive reactions. The patient who gave a negative reaction was a negro who had a definite history of syphilis seven years before. His serum was tested one month later after antiluetic treatment, and with the same result. Two of the cases were of some interest, one an aneurysm of the dorsalis pedis artery and the other a popliteal aneurysm. Seven of the 22 cases gave no history of lues.

This percentage of positive reactions is considerably higher than that obtained by Clough in the first communication from this clinic, who found only 50 per cent positive in 20 cases. The percentage, however, during the years 1909-1911 was much higher and about that obtained the past year. These figures are very impressive and bear out the conviction already held by most clinicians, as to the overwhelming, if not sole, importance of syphilis as the etiological factor in "spontaneous aneurysm."

Tabes and Paresis.

The Wassermann reaction in 17 cases of tabes showed 11, or 64 per cent, positive and 6 negative. Three of these patients gave a negative Wassermann in the serum, while the cerebro-spinal fluid was positive; and three of the patients having positive reactions with their serum showed negative reactions in the cerebro-spinal fluid. Eight of the patients admitted luetic infection; 9 gave no history.

Thirteen cases of general paresis were tested. Twelve, or 92 per cent, of this number were positive. The cerebro-spinal fluid was positive in every case examined (seven), while the blood was negative in seven cases. Nine of the 13 gave a luetic history.

In addition to these diseases of the central nervous system, the reaction was applied to two cases of multiple sclerosis, one case of Friedreich's ataxia, three cases of progressive central muscular atrophy, two cases of bulbar paralysis, and 15 cases of "idiopathic" epilepsy; all with negative results.

Brain Tumor.

This group of cases includes a variety of cerebral tumors—gliomata, hypophyseal tumors and cysts, cerebellar tumors and cysts, and tumors of the spinal cord. The Wassermann reaction was done with the serum of 59 cases, all giving negative results. In seven of these cases the test was also negative with the cerebro-spinal fluid.

Newmark[14] has reported two cases with non-specific tumors of the central nervous system which gave positive reactions. One of these patients died and the tumor proved to be a gliosarcoma of the brain. A complete autopsy, however, was not permitted. The Wassermann reaction was also positive in the cerebro-spinal fluid taken at autopsy. The second patient gave a positive reaction in the blood and was given vigorous anti-luetic treatment despite which symptoms of compression

of the spinal cord increased. The reaction was positive in the cerebro-spinal fluid July, 1911, and on August 31, 1911, an intradural psammona was removed. The Wassermann reaction was negative in the cerebro-spinal fluid during operation and in the patient's serum on September 18, 1911.

Neither of these cases proves that non-specific tumors of the central nervous system give positive reactions, since syphilis was not excluded in the first case and in the second case the vigorous anti-luetic treatment may have been sufficient to cause the disappearance of the positive reaction.

In this connection a case reported by Citron [l.c.] is of considerable interest. This patient was a case of cerebellar ataxia who gave a positive Wassermann. At autopsy the cause of the ataxia was found to be a softening (*Erweichungsherd*), and no signs of luetic changes were found in the brain. Upon further examination, however, the prosector found a well marked aortitis, which, although it had never manifested itself by any symptoms, was nevertheless quite characteristic, and the only definite evidence of luetic infection present.

One patient in our series, who gave a positive reaction with the cerebro-spinal fluid but negative in the blood, was operated upon because of certain symptoms (dizziness, poor vision, and impaired hearing) pointing possibly to a cerebral tumor. Operation, however, showed no tumor but only a chronic serous meningitis, probably of luetic origin.

Diabetes Mellitus.

The Wassermann reaction upon the sera of ten diabetics showed eight negative reactions and two positive reactions. Of the two patients who gave positive reactions, one admitted a very recent luetic infection and the second patient, while denying lues, had, however, symptoms of tabes dorsalis.

Pellagra.

The Wassermann reaction was negative in four cases of pellagra. This number, while too small to admit of definite conclusions, yet agrees with the results of Fox,[15] Carletti,[16] and Vallaidi,[17] who state that the Wassermann reaction is usually negative in pellagra.

Jaundice.

The interesting statement is made by Kaplan [18] that 18 sera containing bile products gave in his hands a positive reaction, although in most of them "syphilis could be absolutely excluded." In our series the Wassermann reaction was performed upon 14 sera from patients who were definitely jaundiced, many showing the most extreme degrees of jaundice. Two patients only of this number gave positive reactions. One of these patients had a gumma of the liver. The second patient, while giving no definite history of lues, had, however, probably been exposed to infection, and gave a markedly positive luetic reaction.

The causes of the jaundice were: Cirrhosis of the liver (seven cases), catarrhal jaundice (two cases), liver necrosis (two cases), gumma of the liver (one case), carcinoma of the bile ducts (one case), and carcinoma of the head of the pancreas (one case).

The Wassermann Reaction of the Cadaver.

Bruck,[l.c.] as is well known from the result of his tests with the sera of cadavers, is very sceptical of their value when positive, and expresses the conviction that *die Syphilisreaktion est ein rein biologisches Phänomen, aber kein kadaveröses.* He found that post mortem sera from patients who had died of various diseases gave positive reactions where the autopsy showed no signs of syphilis. Subsequent investigation of this question shows widely divergent views. Fraenkel and Much [19] found that reactions on cadaver serum corresponded with the pathological diagnosis. Nauwerck and Weichert,[20] as the result of investigations upon the sera of 200 cadavers, also found agreement between autopsy findings and post mortem serum reactions. They state that they have been unable to find any difference "between the living and the cadaver reaction." Krefting,[21] on the other hand, found positive reactions in the sera of cadavers who showed no post mortem signs of lues.

Some of these discrepancies may be due to placing too much reliance upon the post mortem examination, since it is quite possible for patients to have syphilis with a positive Wassermann, and yet present no recognizable lesions at autopsy. For this reason it seems quite necessary to perform the reaction upon the sera both before death and after death, and then by comparison to determine the value of the Wassermann reaction on the cadaver. Nauwerck and Weichert found agreement between 19 sera examined both ante mortem and post mortem, and Schmidt [22] obtained similar results in 32 cases.

The Wassermann reaction has been performed on the sera of 25 patients in this clinic, both before and after death. The serum from the cadaver was obtained by aspirating the heart under sterile precautions and was taken at different periods after death, varying from two hours to two days. The serum was then immediately placed on ice and every specimen was found satisfactory. In these 25 tests there was perfect agreement between ante mortem and post mortem results in every case but one. This patient, who had an abdominal aneurysm, gave a positive Wassermann on admission, but after death his serum showed no complement fixation. He had, however, been under strong antiluetic treatment during his stay in the hospital, which extended over a period of eight months. These results then, agree with those of Nauwerck and Weichert, and Schmidt, in showing the reliability of the test on the serum of cadavers.

Summary.

The past year's experience with the Wassermann reaction in this clinic confirms our faith in the reliability and specificity of this reaction. The only other diseases in which positive reactions have been reported (trypanosomiasis, yaws, scarlet fever, leprosy, and possibly malaria) are either so

easily diagnosed or so uncommon here as to cause no confusion.

Wassermann[8] states that he and his assistants have performed over 10,000 examinations and never yet made a false diagnosis. While the number of patients in our series is much smaller, we feel that we have not made a false diagnosis the past year when the diagnosis of syphilis was placed after the names of 239 patients who showed a positive Wassermann reaction.

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EXCESSIVE THICKENING OF THIERSCH GRAFTS CAUSED BY A COMPONENT OF SCARLET RED (AMIDOAZOTOLUOL).*

By John Staige Davis, M. D.,
Instructor in Surgery, The Johns Hopkins University.

INTRODUCTION.

There has been some skepticism expressed at one time or another in regard to the power of epithelial stimulation claimed for certain of the organic coloring matters (Scarlet Red, Soudan III, Azodolen, Pellidol, etc.), when applied locally to granulating wounds.

To my mind this matter has been settled beyond a doubt, as, during the last four years a number of enthusiastic articles have been published by well-known investigators on the satisfactory use of these substances. These papers almost uniformly report splendid clinical results in hastening the healing of sluggish granulating wounds of varying etiology, and in every situation.

As is usual when a promising new therapeutic agent of this type is brought to the attention of the medical profession, it has been used by many who are not familiar with the principles of wound healing, and who have little knowledge of surgical dressings. If unfavorable results have been obtained by such individuals, I do not believe it is entirely due to the dyestuff.

I have found that these substances will not heal every wound, but, in the majority of instances, when applied with the proper technic, they will cause epithelial stimulation in the edges of the most sluggish wounds, and give a rapid, stable healing.*

The use of these coloring matters has also been objected to, by some who admit their power of epithelial stimulation, on the ground that there might be the possibility of producing epithelial overgrowths having malignant characteristics. It is a well-known fact that malignant degeneration may occur in any chronic ulcer, even though only the blandest dressings be used. The consensus of opinion, deduced from experimental and clinical work, is that there is no more danger of producing malignant growths by the clinical use of these substances than with any other dressing. My own experience in the treatment of a large number of cases has convinced me of this, and I feel no hesitancy in using the organic coloring matters on proper wounds.

I take this opportunity of warning against the indiscriminate use of these substances by inexperienced persons, as considerable harm may be done with them by improperly applied, and too long continued, dressings. There is, occasionally, an overgrowth of epithelium following the use of these dyestuffs, even when the greatest care is exercised but, after discontinuing the stimulating dressing, this overgrowth soon assumes the level and appearance of the normal skin.

The following case shows the epithelial stimulating power of amidoazotoluol to a remarkable degree, and may be of interest:

HISTORY OF CASE.

Admitted to the Union Protestant Infirmary, May 7, 1910.
Diagnosis.—Ulcers following burn.

* Amidoazotoluol is an amidoazo compound employed as an intermediate product, which, when combined with beta-naphthol, forms the Scarlet Red originally used, experimentally, by Fischer,[1] for the production of atypical epithelial proliferations; and was first used, clinically, by Schmieden.[2] Amidoazotoluol was first used clinically by Hayward.[3] It has the formula:

$$C_6H_4(CH_3) - N = N - C_6H_3(CH_3) - NH_2$$

[1] München. med. Wchnschr., 1906, liii, 2041.
[2] Zentralbl. f. Chir., 1908, xxxv, 153.
[3] München. med. Wchnschr., 1909, lvi, 1836, and Deutsche Ztschr. f. Chir., 1911, cxii, 467.

* Johns Hopkins Hosp. Bull., 1909, xx, 176. Ann. Surg., 1911, xxxviii, 702. Boston M. & S. J., 1912, clxvi, 891.

FIG. 1.—Appearance on admission. Ulcer of right arm due to burn 6 months previously. Note exuberant, unhealthy granulations. Grafted skin can be seen on the forearm.

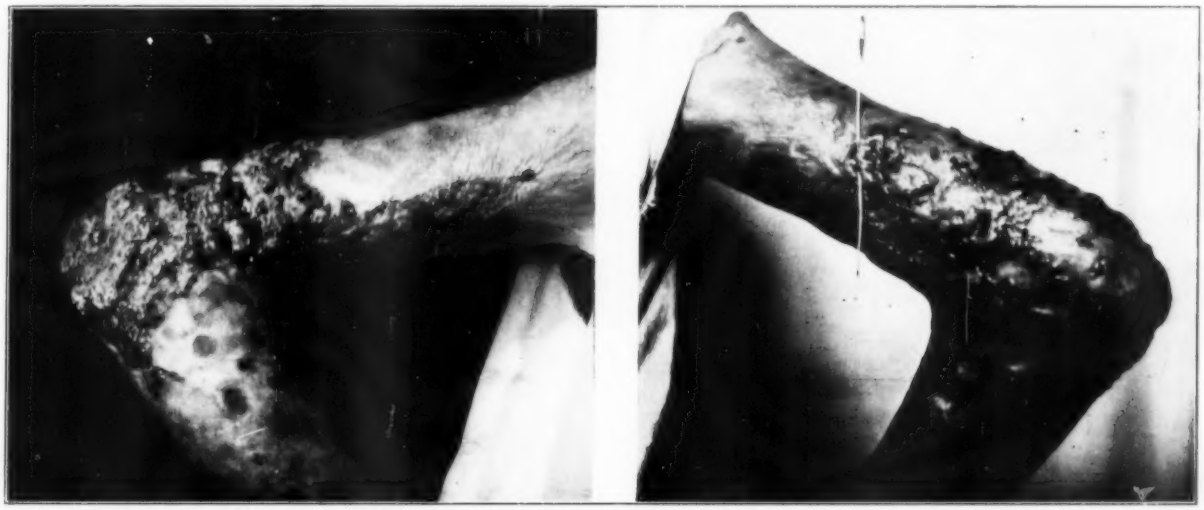

FIG. 2.—(a) Taken July 20, 1910. Note the marked thickening of the Thiersch grafts. The thickened grafts have begun to separate into irregular fungating masses which can be plainly seen.

(b) Taken August 1, 1910. Portions of the thickened grafts have assumed the level of the normal skin. Overgrowth can still be seen in other areas. Note the overgrowth which is attached only by its edges, beneath which a probe is passed. There are a number of similar areas scattered over the arm.

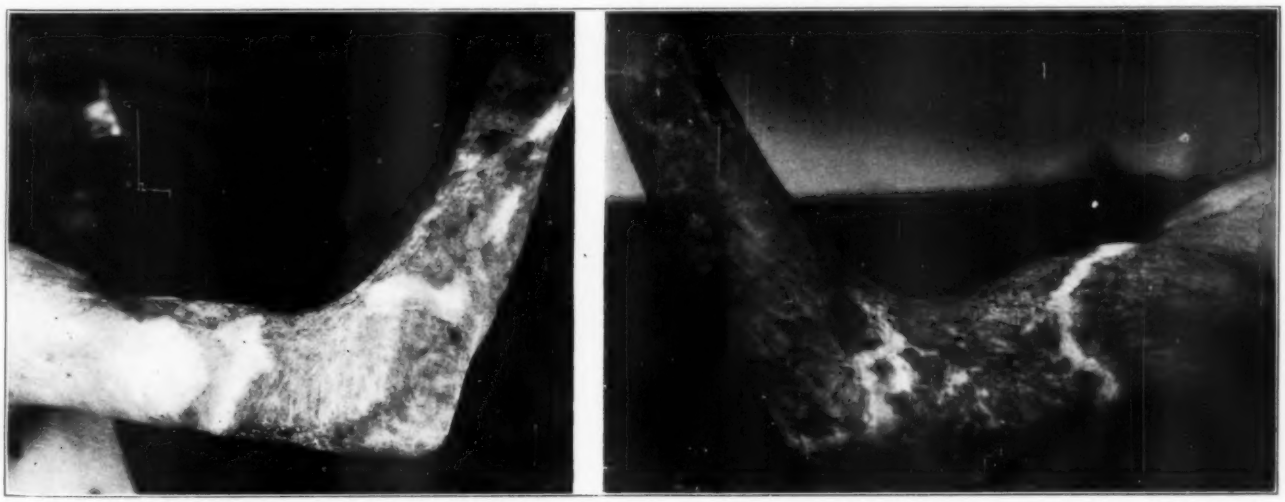

FIG. 3.—(a) Taken January 7, 1911. Five months after discharge. The skin is movable and, for the most part smooth, although several thickened areas can be found. There is considerable pigmentation.

(b) Taken January 4, 1912. Seventeen months after discharge. There is marked blotchy pigmentation of the grafted area. On careful examination of this skin, one or two small, flat thickened areas can be found. There are also a few minute depressions in the skin which are filled with comodo-like masses. Otherwise the skin is normal.

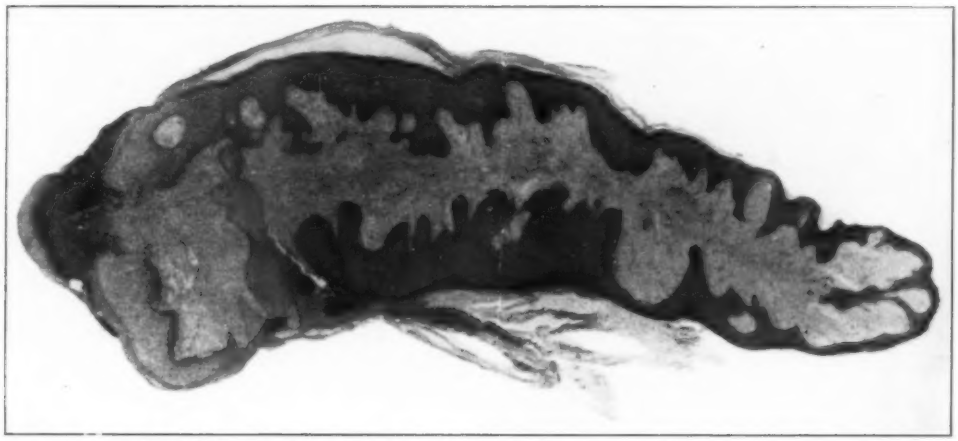

FIG. 4.—(Microphotograph by Schapiro. Zeiss. Obj. AA. Oc. 3.) Section of papillomatous overgrowth. For description see text.

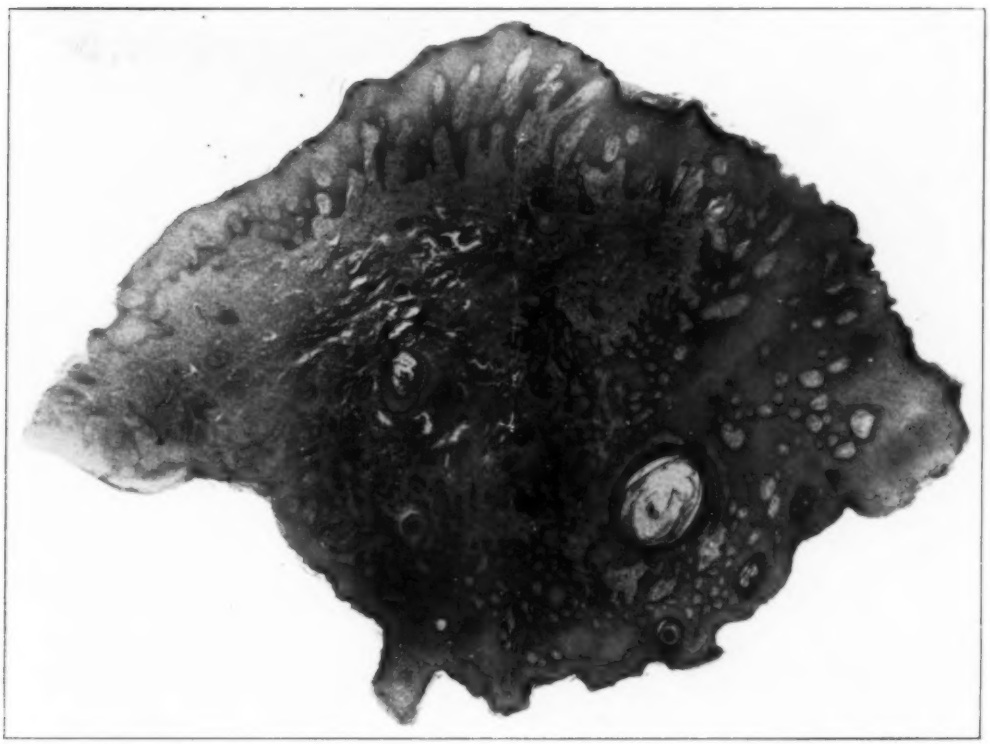

FIG. 5.—(Microphotograph by Schapiro. Zeiss. Obj. AA. Oc. 3.) Section of papillomatous overgrowth. For description see text.

Treatment.—Thiersch grafting in conjunction with amidoazotoluol ointment.

Clinical History.—White man, aged 30 years, engineer.

Family and Personal History.—Unimportant.

Present Illness.—Six months before his admission the patient was severely burned in an oil explosion. The head, neck, both upper extremities and portions of the back and chest were involved, and his condition was serious. He was admitted to the Johns Hopkins Hospital in a critical condition and remained there for five months. While in the hospital skin grafting was resorted to a number of times, and considerable progress was made toward healing. He was discharged, at his own request, before healing was complete, and was referred to the Out-Patient Department for dressings. After several weeks his condition was unimproved, and, as the hospital was crowded, he was sent to the Union Protestant Infirmary, where he came under my care.

Physical Examination.—The patient was anemic and emaciated. There were large unhealed areas on the scalp and on both arms and forearms. I will describe only the ulcer on the right arm, as this is the particular wound to be considered in this report (Fig. 1).

An extensive granulating wound occupied the entire circumference of the lower two-thirds of the arm, including the elbow and upper two inches of the forearm. The wound extended three inches higher on the outer than on the inner side of the arm. On the inner side an area of skin previously grafted extended up from the forearm to the bend of the elbow. The granulations were exuberant, edematous and unhealthy. Practically all the skin of the forearm adjacent to the ulcer had been grafted before the patient came under my care. During the interval between admission to the Union Protestant Infirmary and operation on the right arm the other unhealed areas were grafted.

The granulations of this wound were brought into healthy condition by irrigations, free use of nitrate of silver, balsam of Peru, curved scissors, etc. At the same time very marked progress was also made toward healing by stimulating the wound edges with 4 per cent amidoazotoluol ointment, alternating every 24 to 48 hours with zinc oxide, or boric ointment. The newly formed skin edges were thick and stable, but showed no tendency to overgrowth. As the granulations were flat, firm and rose pink in color, in spite of the rapid stimulation of the wound edges, it seemed advisable to hasten the healing by grafting.

June 28, 1910. *Operation.*—Nitrous oxide-oxygen anesthesia. A number of large thin Thiersch grafts were obtained from the left thigh by the method used at the Johns Hopkins Hospital,* and the grafts were spread on protective and put aside. The thigh was dressed with boric ointment on protective, and the patient was allowed to regain consciousness. The granulating area on the arm was irrigated with salt solution and then dried carefully without causing bleeding. The grafts were buttonholed and applied over a large part of the unhealed area. Rubber impregnated mesh was placed snugly over the grafts, and over this overlapping strips of protective, dry gauze and a bandage.

June 30. The dressings were removed down to the rubber mesh, which was not disturbed. The grafted area was irrigated with normal salt solution and dressed with 4 per cent amidoazotoluol ointment on old linen, over the rubber mesh. This dressing was alternated with boric ointment every 24 hours.

July 12. (After six dressings with 4 per cent amidoazotoluol ointment.) The greater portion of the grafts had taken. Since the last note there had been a remarkable gradual thickening of all the grafts. The surface was smooth but rather uneven, and of a bluish grey color. The appearance was that of an edematous epithelial mass. The thickness varied between ⅛ and ⅜ of an inch. I felt convinced from my experience with occasional overgrowths of wound edges and other grafts caused by the organic coloring matters, that this thickening would begin to subside as soon as the stimulant should be removed. The thickened grafts were dressed with stearate of zinc powder and exposed to the air, in order to promote drying. The amidoazotoluol was discontinued. There was no excessive thickening of the wound edges.

July 20. The thickening of the grafts was still very marked, but the overgrowth had begun to separate into irregular-shaped fungating masses. When a section was removed for microscopic examination, there was little pain but profuse bleeding (Fig. 2).

July 22. Thiersch grafts from the left thigh were placed on the remaining undisturbed granulations and dressed with salt solution over the rubberized mesh.

July 29. All the grafts last applied had taken, and *were of normal thickness*, no amidoazotoluol having been used. The first grafts had resumed, in some places, the appearance of normal grafted skin. In others, several areas had assumed a papillomatous formation. Some of these were of the size of a pea, and were adherent to the underlying clear skin by a small pedicle. Others were flattened mushroom-like masses, with overhanging edges, while other areas were adherent here and there along their edges, and not elsewhere, so that an instrument could be passed freely underneath them. Some of the thickened areas were 1½ inches in diameter, a single portion comprising about one-half of this, and the rest being made up of closely set papillæ, which extended above the surface of the skin from ⅛ to ⅜ of an inch.

Several of these areas were cut off, and normal looking skin was found beneath, except for bleeding at the points of attachment. Here and there masses of cheesy secretion could be pressed from under the overgrown areas, and this had the typical odor of the contents of an atheromatous cyst. Microscopic examination showed this to be made up of epithelial debris.

August 13. Some of the papillary overgrowths had been removed, and many others had dried out and fallen off, as the blood supply of the pedicles was gradually occluded. Those which remained were much less prominent than at the last note. A large part of the thickened grafts had assumed the level of the normal skin, which was of a pinkish color. These level areas gave no evidence of having undergone excessive epithelial stimulation.

The patient was discharged in excellent physical condition, and with practically complete healing of all his lesions.

October 15. The greater part of the grafted skin on the right arm was smooth, but here and there were scattered a few small flat, dry papillomatous overgrowths. These growths received their nourishment through very small pedicles, between which the formation was bridged. The patient was working at his usual occupation.

January 7, 1911. Practically all of the papillomatous growths had disappeared, and the area was covered with smooth, solid skin (Fig. 3).

January 14, 1912. The arm was covered with a stable, movable skin, which was heavily pigmented. On careful examination one or two very small thickened areas could be found on the inner side of the arm. There were also several comedo-like masses which filled minute pockets in the skin.

January 5, 1913. The condition of the skin had not changed since the last note.

Histology.—(Microscopic examination by Dr. Joseph C. Bloodgood*) Fig. 4). There was an oblong piece of tissue with a central zone of edematous connective tissue surrounded by epidermis. The papillary bodies of the epidermis were present. These papillary bodies varied in size and shape; they were larger and more irregular than in the normal epidermis. In some places the hornified epithelium on the surface was more marked than normal.

* Ann. Surg., 1909, vol. 543.

* I take this opportunity of thanking Dr. Bloodgood for the microscopic study.

Corresponding to these areas the epidermis was thicker than in areas in which the hornification was less. The epidermis differed from normal in the fact that the basal cell was not so distinct in its morphology, and in places the downgrowth of epidermal epithelium was more irregular than normal. We would speak of it as atypical. In one end of the section the central connective tissue looked myxomatous or edematous. In the faintly stained intercellular substance there were a few round and stellate connective tissue cells, resembling, therefore, myxomatous tissue. Here and there was a lymph vessel filled with leucocytes. At the other end of the section there was a defect in the epidermal covering, and this was filled with lymphoid-cell granulation tissue. This granulation tissue grew out from a narrow isthmus in the epidermis, and projected over the surface of the epidermis, like a fungous ulcer. On each side of the granulation tissue in the defect in the epidermis, the epithelial cells were extending irregularly into the granulation tissue. The cell proliferation in the granulation tissue was of the type of the transitional and squamous cell. This histological picture was somewhat similar to that seen in the beginning of carcinoma.

The other piece of tissue (Fig. 5) had the appearance of having been cut on the bias. The central zone of connective tissue was smaller, the epidermis much thicker, and the section seemed to be horizontal through the papillæ rather than vertical. There were also a few cavity formations in the epidermis, filled with hornified epithelium, which had the appearance of the so-called inclusion dermoid cysts. In the connective tissue of this section, there were numerous endothelium-lined canals filled with blood, probably young capillaries, and some more dilated similarly lined spaces filled with blood, which may have been veins. There were also some dilated endothelium-lined spaces which suggest lymphatics.

The entire picture, therefore, suggests unusual epithelial activity. That is, the healing process of epidermization was going on very actively; one would naturally conclude, perhaps too actively, or, as Adami would express it, "over-sufficient." The possibility of producing a definite malignant epithelial growth from such stimulation, as has been observed in x-ray and radium keratosis, should be borne in mind. This possibility is illustrated in the character of the epithelial overgrowth into the granulation tissue filling a defect in the epidermis as noted above. Here the cells were not growing as in normal epidermization in which the downgrowth was always composed first of a basal-cell layer, but, instead, the transitional and squamous cells were proliferating irregularly into the granulation tissue, as in carcinoma. But these cells as yet have not assumed the abnormal morphology seen in cancer.

REMARKS.

The microphotographs, especially Fig. 5, show a condition which resembles very closely the sections of the atypical epithelial proliferations produced by injecting scarlet red oil, subcutaneously, under pressure into a rabbit's ear.* These experimental tumors never show a tendency to independent aftergrowth, and persist only as long as the injections are continued and the scarlet red remains in the tissues.

The epithelium of this patient seemed to be particularly responsive to the stimulation of amidoazotoluol, and these thickened grafts present the most remarkable condition of overgrowth which has come under my observation.

It is interesting to note that Thiersch grafts which were subsequently applied to unhealed portions of the same wound, under exactly the same conditions, but without being dressed with amidoazotoluol, were not thickened.

There was also great thickening of the deep pinch grafts placed on the undisturbed granulations of the ulcer on the scalp, which had been treated with amidoazotoluol before and after the application of the grafts. There was no such thickening, however, of similar grafts placed on undisturbed granulations, when not dressed with amidoazotoluol. There was distinct overgrowth of epithelium "pebbly formation" on the thigh, when the area from which the Thiersch grafts were removed was dressed with amidoazotoluol ointment. Another area on the thigh from which Thierch grafts were taken, but which was dressed with boric ointment, showed no "pebbly formation."

The patient has been under observation for over two years and a half since his discharge from the hospital, and there is no sign of malignant degeneration anywhere.

This condition is unique, and I can find no report in the literature of a similar case. It demonstrates beyond a doubt the epithelial stimulating power of amidoazotoluol. It also seems to show that although this stimulation is excessive, there is no tendency to subsequent malignant degeneration.

* F. H. Helmholz. Johns Hopkins Hosp. Bull., 1907, xviii, 365. Fig. 2, Exp. Ia.

THE SUBSEQUENT HISTORY OF ONE THOUSAND PATIENTS WHO RECEIVED TUBERCULIN TESTS.

By Johanna Gelien, M. D.,

and

Louis Hamman, M. D.,

Associate in Medicine, The Johns Hopkins University.

In the Archives of Internal Medicine (1910, VI, 690) Hamman and Wolman reported the results of the application of the cutaneous and conjunctival tuberculin tests to one thousand patients coming to the Phipps Dispensary for Tuberculosis of The Johns Hopkins Hospital. From an analysis of the results certain conclusions were drawn as to the value of these tests in diagnosis. For this purpose the patients were divided into six groups, the division being made upon the clinical evidence without reference to the outcome of the tests. It is important for a proper appreciation of the present study to bear in mind the data upon which the classification rested and the data are therefore repeated.

Group I. *Non-tuberculous.*—This group included those patients who had no symptoms or signs of tuberculous disease,

and those with symptoms which might have been readily accounted for by some disease other than tuberculosis.

GROUP II. *Doubtful.*—This group included the patients presenting symptoms or physical signs that might be due to tuberculosis and for which no other satisfactory explanation could be given. The symptoms and signs, however, were not sufficiently convincing to establish the diagnosis definitely.

GROUP III. *Probable.*—This group included patients with symptoms or physical signs so suggestive of tuberculous disease that clinically the diagnosis was in every way reasonable. However, complete confirmation had not been possible. We made a special group of these patients to free the incipient group as far as possible from the influence of the personal equation.

GROUPS IV, V AND VI.—These groups included the definitely tuberculous cases. As tuberculous were included cases with tubercle bacilli in the sputum and those affording only the strongest clinical evidence of tuberculosis. Cases about which clinical observers might have even a slight doubt were placed in the doubtful class which was therefore very large. The tuberculous cases were divided into incipient, moderately advanced and far advanced, according to the demands of the classification proposed by the National Association for the Study and Prevention of Tuberculosis.

It is important to add further that the examinations upon which the diagnoses in the one thousand cases were based were made in a busy out-patient department by a staff of twelve physicians. Some of these physicians possess experience and skill in the diagnosis of pulmonary tuberculosis far above the average, while a few have these qualities in but a mediocre degree. The classification, therefore, is not to be viewed as the interpretation of physicians of exceptional insight and finesse.

Our object in seeking the after history of these individuals tested with tuberculin was to throw light upon a number of points connected with the dispensary work. In the first place it might serve as further evidence of the value of the tuberculin tests. Many of the doubtful cases reacted to tuberculin. Has a larger percentage of those who reacted become manifestly tuberculous than of those who failed to react? Again, it has been suggested that in tuberculous patients the presence or absence, indeed the intensity of the tuberculin reaction, has important prognostic significance. The relation of the tests to the patient's condition two years later would settle this point. Yet again, it would furnish the opportunity to repeat the tests upon a large number of patients and thus determine the duration of the hypersensitiveness occasioned by a conjunctival instillation. But most important of all, we wished to use the subsequent history of tested patients as a control of the classification itself. A few words of explanation are necessary in this connection.

There is as wide an individual difference of opinion as of skill in the diagnosis of early pulmonary tuberculosis. Although a number of observers may be in accord upon the clinical evidence, still they may differ widely in the interpretation put upon it. A patient with suggestive symptoms and suggestive physical signs will be classed uncompromisingly as tuberculous by one, as possibly tuberculous by another, as not tuberculous by a third. By "tuberculous," we mean a clinical not an anatomical diagnosis, and imply the therapeutic consequences that flow from the diagnosis: namely, if tuberculous the patient needs energetic treatment, preferably admission to a sanatorium; if doubtful, careful and prolonged observation; if not tuberculous, dismissal. Inclination to accept or urge one of these three diagnoses represents a certain attitude towards tuberculosis work and is greatly influenced by mental bias. A number of physicians are sceptical of and some irritated by the diagnostic refinements of tuberculosis workers. They miss the spirit of the work and therefore misinterpret its aim. They will have none of the ultra-refined specialism, and the symptoms and lesions must be gross before they bend their stubborn judgment. Unquestionably helpful diagnoses are thus overlooked. At the other extreme stand many sanatorium physicians. To obtain satisfactory results from treatment they justly clamor for early cases, and their zeal and enthusiasm naturally color their judgment. They lean upon a forceful argument, for in the presence of indefinite symptoms and signs it is safer to say a patient has tuberculosis and then cure him with six months' treatment in a sanatorium than to hesitate and later find, perhaps, that valuable time has been lost. It can do no harm, they urge, to treat a few patients needlessly if thereby you prevent hundreds of others from going on to hopelessly advanced disease. We will not stop to analyze these arguments which are interesting in many ways. We merely suggest that a possible fallacy lurks behind the "few." Between these two extremes stands the large body of conservative tuberculosis students. They do not see advancing destruction lurking behind each slightly impaired percussion note, each rude inspiration, and yet experience has taught them to be wary and circumspect in judging. They demand reasonable proof before they pronounce a patient tuberculous while they regard every unusual feature with grave suspicion. Indeed, they are so permeated with suspicion that they naively transfer this attitude to the patients and speak of them as "suspicious," thus clothing with their own mental bias many entirely unsuspecting and confiding individuals.

We have fought out this question in the Tuberculosis Dispensary during the past eight years, and as a whole we have come to assume a very conservative attitude towards the early diagnosis of pulmonary tuberculosis. Our large group of doubtful or suspicious cases attests this. If, then, a large number of our doubtful cases have subsequently become manifestly tuberculous, we have erred on the side of being too conservative; whereas if, under the ordinary conditions of life, nearly all have remained well or have not become more definitely tuberculous than they were before, our standpoint is entirely justified. Without knowing the results of this investigation, we may at once predict that a certain number of the doubtful cases have become tuberculous. Many of the patients were seen only once, and then often hurriedly, and as we have before remarked, some of the examinations were not unusually skilful. Although all the diagnoses were carefully reviewed, it is often difficult to reach a satisfactory conclusion from the data furnished by another especially when, as was often the case, these

data are incomplete. To keep our tuberculous group as irreproachable as possible we have made it a rule to place in the doubtful group any case not frankly tuberculous. It therefore includes many cases that would have been diagnosed definitely tuberculous had they returned for further observation.

The patients were sought by personal visits and by letter. Our nurses were indefatigable in their efforts to trace as many of the patients as possible and we wish to thank Miss Gould and Miss Donaldson, of the dispensary staff, and Miss LaMotte, directress of the municipal tuberculosis nurses, for their enthusiastic aid.

TABLE I.—THE PRESENT CONDITION OF 632 PATIENTS CLASSIFIED FROM THREE TO FOUR YEARS BEFORE.

	Sought.	Reports.	Well.	Not improved.	Became tuberculous.		Death not from tuberculosis.
					Living.	Dead.	
Not tuberc...	188	110	72—65%	31—28%	3— 2.7%	1—0.9%	3—2.7%
Doubtful.....	429	258	176—68	57—22	7— 2.7	9—3.5	9—3.5
Probable.....	78	47	29—61	.....	11—23	7—15	.....
Tuberculous							
Stage I	35	21	13—62	4—19	.....	3—14	1—4.7
Stage II ...	79	47	15—32	10— 21	.....	22—47	.....
Stage III...	191	149	11— 7	10— 6.7	.....	128—86	.....

Table I shows the general results of the investigation. It will be noted that of 110 patients originally classified as non-tuberculous from whom reports have been obtained, four have become definitely tuberculous. A very brief account of these cases is given.

No. 3560, L. L., white male, aged 11 years, came to the dispensary on November 4, 1908, complaining of cough and loss of weight. Family history was negative, and there was no history of exposure to tuberculosis. Child had had whooping-cough, measles, chicken-pox and mumps and frequent attacks of bronchitis.

Present illness began on October 27, 1908, with cough and fever. He was in bed two days and then gradually grew better.

Patient was a fairly well nourished boy of delicate appearance. The cervical glands were just palpable. There was slight impairment at the right apex, with roughened breath sounds and prolonged expiration; no râles heard. Heart and abdomen were negative.

The 1 per cent and the 5 per cent conjunctival and the cutaneous tests were all negative.

Patient returned to the dispensary on January 25, 1912, saying that he had been well since his previous visit, except that for three years there had been a swelling in the left side of the neck. This grew larger and smaller at intervals.

The examination of the chest showed the same slight signs at the right apex as before.

Throat examination showed the presence of adenoids and enlarged tonsils. A surgical consultation agreed with the diagnosis of tuberculous cervical glands.

The 1 per cent conjunctival and the cutaneous tests were positive. Wassermann reaction negative. X-ray examination showed marked mediastinitis, but no definite pulmonary lesion.

No. 4634, R. R., colored girl, aged 15 years, came to the dispensary on July 9, 1909, complaining of cough. Family history, as far as it could be obtained, was negative. There was no history of exposure to tuberculosis. The past history gave nothing of importance in relation to the illness. Six years before admission the patient had had a cough, for which she had been treated in the dispensary. The cough subsided and she was then well until three weeks before admission, when the cough returned.

Examination showed a well nourished colored girl, with slightly enlarged cervical glands, marked pyorrhea alveolaris and enlarged tonsils. The lungs showed slight impairment above and below the right clavicle and in the supraspinous fossa. Breath sounds over this area were rough and expiration prolonged. Numerous coarse, moist râles and a small number of fine râles heard over the whole side. Over the left back there was slight impairment below the angle of the scapula and numerous fine moist râles over the area of impairment. Examination otherwise negative.

The 1 per cent and the 5 per cent conjunctival and the cutaneous tests were negative.

At the end of a month, the râles had completely disappeared, and the slight impairment above and below the right clavicle and in the right supraspinous fossa was the only abnormality made out on examination.

Patient returned to the dispensary on May 3, 1911, with pleural effusion on the left side.

No. 4835, E. P., white woman, aged 52 years, came to the dispensary for examination on August 20, 1909, because she had been nursing a tuberculous patient for 13 months. She had had a little cough occasionally. Family history and past history were negative. Had always been a healthy woman.

Examination showed a well nourished woman, with indefinite signs at the right apex, namely, slight dulness and roughened breath sounds.

The 1 per cent and 5 per cent conjunctival and the cutaneous tests were negative.

Patient returned to the dispensary on October 3, 1910, having lost a few pounds in weight and feeling generally not so well as at the first visit.

Examination showed an advanced tuberculous lesion, involving both lungs.

Patient entered the State Sanatorium. She died of pulmonary tuberculosis on December 27, 1911.

No. 5072, J. B., white male, aged 39 years, came to the dispensary on November 10, 1909, complaining of nose trouble. One brother had died of tuberculosis. He had been exposed to the disease in his workshop. He had been always healthy. For many years he had had nasal catarrh, and some cough and expectoration.

Patient was a fairly well nourished man, in good general condition.

Examination showed slight impairment above and below the right clavicle and in the supraspinous fossa. Breath sounds were rather suppressed and a few fine râles were heard scattered over the upper front and back. The percussion note was impaired on the left side, above and below the clavicle and in the supraspinous fossa. Breathing was very distant and suppressed. A few fine râles at the third rib in front and over the upper back.

The 1 per cent and 5 per cent conjunctival tests were negative; the cutaneous test positive.

The pulmonary condition was considered to be emphysema and chronic bronchitis, and as the nasal symptoms predominated, the patient was sent to the throat physician for operation. Examination showed a deflected septum with hypertrophy of both turbinates, largely obliterating the nasal cavity.

Patient returned to the dispensary on September 7, 1912. After his first visit he had had cough and expectoration at intervals. The nasal symptoms had not been completely relieved by the operation.

Examination showed that the impairment and change in breath sounds made out at the first examination had increased and the number of râles had also increased. The 5 per cent conjunctival and the cutaneous tests were markedly positive. The sputum contained tubercle bacilli. Patient's general condition was good. Was admitted to a sanatorium.

In the group classified as doubtful, 16 of the 258 patients of whom we have reports have become definitely tuberculous.

We have shown a special interest in this group and to make the nature of these cases clear we briefly state the facts concerning them.

No. 2352, M. M., white female, aged 52 years, came to the dispensary on January 10, 1908, complaining of bronchial trouble. Family history was negative. Patient had had pleurisy 12 years before; had had bronchitis, with cough, expectoration and dyspnea for many years. Symptoms had been getting worse for a year before admission. Patient's general condition was satisfactory.

Examination of the lungs showed impairment over both upper lobes, with diminished intensity of the breath sounds and blowing expiration. Numerous sonorous and sibilant râles over both sides.

Three sputum examinations were negative. The 1 per cent conjunctival test was negative; the cutaneous test, positive.

The case was regarded as one of chronic bronchitis, with tuberculosis as a possibility.

Patient returned to the dispensary in May, 1912. Although the general condition had remained good, examination at this time showed marked bilateral tuberculous involvement. The 1 per cent conjunctival and the cutaneous tests were positive.

No. 3404, M. C., white female, aged 63 years, came to the dispensary on September 24, 1908, complaining of cough that had been present, off and on for several years. The family history was negative. The daughter-in-law had tuberculosis. Nothing of interest in the past history.

The patient was a fairly well nourished old woman, seven pounds under weight.

The lungs showed impairment above and below the right clavicle and in the supraspinous fossa, with harsh exaggerated breath sounds, and a few fine râles above and below the clavicle. Numerous sonorous and sibilant râles throughout both lungs.

One sputum examination was negative. The 1 per cent conjunctival test was negative, the 5 per cent conjunctival and the cutaneous tests were positive. The case was diagnosed as bronchitis probably with pulmonary tuberculosis.

The patient came to the dispensary off and on during the following year. On April 3, 1912, she had lost ten more pounds in weight, cough was more troublesome than it had been and examination showed a definite increase in the pulmonary lesion, with numerous moist râles.

August, 1912. The 1 per cent conjunctival test was positive. Patient still comes to the dispensary and is in fairly good condition.

No. 3524, L. M., white female, aged 41 years, came to the dispensary on October 23, 1908, complaining of pain in chest and back, and slight cough. Family history was negative. Patient had been helping to nurse a tuberculous patient. She had had measles and rheumatism. She was rather thin and pale and six pounds under weight.

Examination showed dulness over right upper front to second rib with increased transmission of voice sounds and moist râles from the second to the fourth rib. On the left, the note was impaired to the third rib, the breath sounds blowing and fine râles above and below the clavicle and at the base.

The sputum examinations were negative. The 1 per cent conjunctival and the cutaneous tests were negative. Diagnosis of probably pulmonary tuberculosis was made.

Examination on November 3, 1911, showed an extensive bilateral tuberculous lesion. Patient had tubercle bacilli in sputum, and the 1 per cent conjunctival test was positive.

No. 3552, J. N., white male, aged 74 years, came to the dispensary on October 30, 1908, complaining of sore throat and cough. Had always been a healthy man. Illness began three months before coming to the dispensary, with hoarseness, cough, profuse expectoration and loss of weight.

The patient was an emaciated old man, with the physical signs of emphysema and bronchitis, without signs of localized disease. The 1 per cent conjunctival test was positive.

Patient made but two visits to the dispensary, and was then lost track of. On June 6, 1912, the nurse reported that patient had died two years previously of pulmonary tuberculosis.

No. 3621, R. R., white female, aged 15 years, came to the dispensary on November 17, 1908, complaining of being nervous and easily tired. Patient spoke English with difficulty, so no satisfactory history could be obtained; however, she had apparently been well until one month before. She had no cough or expectoration.

Patient was of healthy appearance, and no definite signs of pulmonary disease were made out. The 1 per cent conjunctival and the cutaneous tests were positive.

On May 5, 1911, patient returned to the dispensary, complaining of loss of appetite, cough and sweating. She had lost five pounds in weight and examination showed impairment at the right apex, with modified breath sounds and a few râles after coughing.

Patient was subsequently admitted to a sanatorium and left much improved. She now has signs of a bilateral apical lesion, and symptoms pointing to hyperthyroidism.

No. 3813, H. S., white female, aged 33 years, came to the dispensary on January 13, 1909, complaining of stomach trouble. There was no history of tuberculosis in family. Past history of patient not important. She had been ill one year with pain in the stomach, poor appetite and growing weakness. She was a pale, nervous woman, with rapid pulse.

Pulmonary examination showed some impairment at both apices, with harsh breathing, and a few râles at the left apex.

Abdomen was somewhat distended and very tender, but no satisfactory abdominal examination was made at that time.

The 1 per cent conjunctival test was negative, the cutaneous test positive.

Subsequently patient was admitted to the hospital, where a diagnosis of tuberculous peritonitis was made.

Patient died on October 10, 1909.

No. 3847, W. B., colored man, aged 37 years, came to the dispensary on January 22, 1909, complaining of cough, pain in chest, and hemoptysis. Family and past history not important. His symptoms began six months before coming to the dispensary, following a cold.

Examination on admission showed marked involvement of the right upper lobe.

Two sputum examinations were negative. The 1 per cent conjunctival test was negative, the cutaneous test positive.

Patient continued coming to the dispensary, the signs of pulmonary involvement increased, and in September, 1910, there was definite tuberculous involvement of both lungs.

Patient died in February, 1912, no doubt of pulmonary tuberculosis.

No. 4033, R. K., white female, aged 27 years, came to the dispensary complaining of pain in the left side and blood spitting. Family history and past history were unimportant. Had always been a healthy girl.

Two weeks before coming to the dispensary, after drinking a glass of cold water, patient spat up a little blood. She had had no cough and no expectoration.

Patient was a well nourished girl of normal weight, showing no abnormality on examination other than a few râles in the left inter-scapular area.

Two sputum examinations were negative. The 1 per cent conjunctival and the cutaneous tests were pcsitive.

The patient made no further visits to the dispensary and although requested to return for observation, refused to do so, saying that she was quite well, had gained in weight and was working hard. She continued to feel well until March, 1912, when

she had grip. She returned for examination in May, 1912, showing a marked involvement of the right upper lobe and a slight lesion in the left upper lobe. Tubercle bacilli were found in the sputum.

No. 4561, P. P., white female, aged 25 years, came to the dispensary on June 22, 1908. She came for examination, saying she had absolutely no pulmonary symptoms.

She was a well nourished woman. Examination showed impairment above and below both clavicles and in the supraspinous fossæ with prolonged, blowing expiration, and fine râles above and below the clavicles.

The 1 per cent and the 5 per cent conjunctival tests were negative.

The note was made: "One would certainly conclude from the signs that patient has a biapical tuberculous lesion. Absence of all symptoms and of tuberculin hypersensitiveness do not lend strong support to this view."

On April 29, 1911, patient again came for examination and the pulmonary signs were more definite than at the first examination. The 5 per cent conjunctival test was positive.

Patient has remained in good condition. She has had no sputum for examination.

No. 4685, H. S., white male, aged 21 years, came to the dispensary on July 19, 1909, complaining of cough. Nothing of importance in the family or past history. He dated his illness from four months before admission when he had caught a cold. He had been coughing since then, and had lost some weight.

The patient was emaciated and pale, and showed physical signs indicating a lesion in both the left and the right upper lobes.

The 1 per cent and the 5 per cent conjunctival tests were negative, the cutaneous test positive.

A diagnosis of probably pulmonary tuberculosis was made, condition marked "far advanced" and prognosis "bad". On February 15, 1912, a report was received, stating that the patient had died of tuberculosis one year before.

No. 4642, R. D., colored man, aged 46 years, came to the dispensary on July 12, 1909, complaining of cough, shortness of breath, dizziness and hemoptysis. He had been ill for two weeks.

He was rather poorly nourished and dyspnœic and showed a pleural rub at the left base. The lung examination was otherwise negative.

The 1 per cent and the 5 per cent conjunctival tests were negative, the cutaneous test positive.

On September 15, 1911, patient returned to the dispensary, having been fairly well until six weeks before. At that time, cough and expectoration became well marked, and he had fever, chills and dyspnœa. Respirations were very rapid and labored.

Pulmonary examination showed marked involvement of both upper lobes. Tubercle bacilli were found in the sputum.

No. 4690, H. W., colored man, aged 35 years, came to the dispensary on July 19, 1909, complaining of throat trouble and loss of voice. He had had cough and expectoration for six months. He was fairly well nourished, had a temperature of 100.8°F., and pulmonary examination showed incomplete consolidation of the right upper lobe with few râles.

The 1 per cent conjunctival test was negative, the 5 per cent conjunctival and the cutaneous tests, positive.

The patient made no further visits to the dispensary.

A report states he died of pulmonary tuberculosis November 29, 1909.

No. 4886, R. C., colored man, aged 27 years, came to the dispensary on September 7, 1909, complaining of shortness of breath and cough. Symptoms had been present for four months.

Examination showed a well nourished colored man of healthy appearance, with a little apical impairment, harsh breathing, and numerous moist râles over both chests. A diagnosis of chronic bronchitis was made, possibly with tuberculosis.

The 1 per cent conjunctival and the cutaneous tests were negative.

The patient made no further visits to the dispensary, but the nurse reports that he died in January, 1910, having had hæmorrhages and a bad cough.

No. 4904, M. B., white man, aged 67 years, came to the dispensary on September 14, 1904, complaining of pain in the abdomen. He had had cough and expectoration for some time; the abdominal pain was of 12 weeks duration.

He was an emaciated man, showing on examination bilateral apical impairment, with blowing breath sounds, and a few coarse, moist râles over both fronts. The case was diagnosed bronchitis, and probably pulmonary tuberculosis.

Two sputum examinations were negative. The 1 per cent and the 5 per cent conjunctival and the cutaneous tests were all negative.

Patient made several visits to the dispensary, gained in weight and said that the symptoms had been relieved.

Nurse reports that patient died of pulmonary tuberculosis in January, 1912.

No. 4923, F. W., white female, aged 14 years, came to the dispensary on September 20, 1909, complaining of cough and night sweats. She had had a cough for one month.

Examination showed some impairment over the right upper lobe, with coarse dry râles throughout the right side.

The 1 per cent conjunctival test and the cutaneous test were positive.

Patient reported one week later, saying that she felt much better. There is no further note until the report from the nurse, which states that the patient died of pulmonary tuberculosis in April, 1910.

No. 4934, E. W., white female, aged 38 years, came to the dispensary on September 23, 1909, complaining of cough. She had had cough off and on for a great many years. Nothing of importance in family or past history.

The patient was a well nourished woman, and looked to be fairly healthy. Pulmonary examination showed a little impairment over the right upper lobe, with suppressed breath sounds, and slightly blowing expiration. A few coarse râles were heard generally over the right side. A provisional diagnosis of chronic bronchitis was made.

The 1 per cent and the 5 per cent conjunctival and the cutaneous tests were all negative.

On September 29, she complained of soreness in the throat. A laryngeal examination was made on October 13, and a diagnosis of laryngeal tuberculosis made.

Patient died of pulmonary tuberculosis on April 10, 1911.

It is apparent that the diagnostic errors here recorded are due in most instances to errors in the interpretation of symptoms and physical signs rather than to a lack of ability in eliciting the signs. The wonder is that in some of the cases (Nos. 3524, 3847, 4685, 4690) there was any hesitation about classifying them at once as tuberculous. The occasion for such hesitation is not apparent in the records, but at the time there must have been some ground for it. Only two of the cases (Nos. 3621, 4023) presented such slight objective evidence of pulmonary disease that in spite of the symptoms the diagnosis was held open. Note the six times repeated classical error of calling a chronic pulmonary tuberculosis in the aged, chronic bronchitis. (Nos. 2352, 3404, 3552, 4886, 4904, 4934.)

We need make no other comment upon these cases than to add that to our mind the after history of our doubtful group fully substantiates the conservative attitude we have taken towards the early diagnosis of pulmonary tuberculosis. The

early diagnosis of pulmonary tuberculosis is more a matter of clinical experience and judgment than of unusual skill in eliciting slight abnormalities in the pulmonary physical signs. Whereas skilful pulmonary examinations require a natural gift that has been cultivated by assiduous application, the observation of symptoms needs only the training that every careful physician acquires in his daily work. It seems to us, therefore, that in attempting to improve the diagnostic acumen of general practitioners towards pulmonary tuberculosis, more emphasis should be laid upon the observation of symptoms than upon the pulmonary examination. To carry out the former is within the reach of all, while to do well the latter will ever be a goal unattained by most of them. It should be urged particularly that when obvious symptoms are present their importance be not subverted by a so-called negative examination.

In the probable and incipient groups it will be noted the same proportion of cases in each group are well and have died of tuberculosis. This we anticipated, since, as we have stated, we devised the probable group as an expedient for cases that we regarded as early pulmonary tuberculosis, but where the evidence for the presence of the disease was not convincing. We may assume from the after history of the patients in the two groups that nearly all of the probable cases were in fact instances of early pulmonary tuberculosis.

It will be seen that many of the patients who had definite tuberculous disease are classed as well. By well, we mean that the patients report that they feel well. It is not to be understood in any sense as meaning that they are cured. Perhaps a few examples will make the matter clear.

No. 964, J. G., white male, aged 22 years, came to the dispensary on July 22, 1906, complaining of cough and pain in the chest. Illness had begun five years before, with hæmorrhages. His father had died of tuberculosis.

The patient was a fairly well nourished man, without marked constitutional symptoms. There was involvement of most of the right lung. Tubercle bacilli were found in the sputum.

On November 9, 1909, examination showed that the process had extended to the left side, the whole upper left lobe being involved. The general condition had suffered, he was pale and had lost weight.

The 1 per cent conjunctival test and the cutaneous test were both positive.

Patient was admitted to Eudowood Sanatorium, and after discharge from the sanatorium worked at the Farm Colony until February, 1912. He was then discharged from the institution as arrested.

No. 4885, A. P., white male, aged 25 years, came to the dispensary on September 7, 1909, complaining of blood spitting. He had had cough off and on for a year.

The patient was a pale, thin man, 16 pounds under weight. There was involvement of both upper lobes, and a large portion of the right lower lobe.

The 1 per cent conjunctival test was negative, the 5 per cent conjunctival and the cutaneous tests were positive. Tubercle bacilli were found in the sputum.

Patient was put to bed until temperature came to normal, and then started on tuberculin treatment. There was some improvement in the general condition and in the physical signs. Fewer râles were heard in the lungs.

In May, 1911, he entered Eudowood Sanatorium and was there three months. Patient then moved to the country and a letter of October 2, 1912, states that he is feeling better than he has felt for a long time; has no cough, appetite is good and he has gained in weight.

No. 5239, W. Z., white male, aged 41 years, came to the dispensary on December 21, 1909, complaining of cough. He dated his illness from April, 1909, when he had pneumonia and was confined to bed for four weeks. Had had cough ever since then.

Patient was a fairly well nourished man, but very pale and of sallow complexion. There was marked involvement of both sides, with a large cavity in the left upper lobe.

The 1 per cent conjunctival and the cutaneous tests were positive. Tubercle bacilli were found in the sputum.

Patient entered Eudowood Sanatorium in the spring of 1910. A letter from his wife dated August 15, 1912, says that patient is now living in the country on a small farm and is strong enough to work it himself. He still has some cough and expectoration, but his general condition is good, and he has gained somewhat in weight.

As a parting glance at Table I, we invite inspection of the columns headed "well" and "deaths from tuberculosis." The gradual increase in the proportionate number of deaths in the different groups is striking. The figures suggest how futile are our efforts to treat successfully poor patients with pulmonary tuberculosis, advanced beyond the incipient stage.

TABLE II.—THE AFTER HISTORY OF PATIENTS IN RELATION TO THE TUBERCULIN TESTS.

		Became tuberculous.	Did not become tuberculous.
Not tuberculous.	Reacted to 1% conjunctival test.	0— 0 %	1—100%
	Reacted to 5% conjunctival test.	0— 0	5—100
	Reacted to the cutaneous test...	1— 3	31— 97
	Negative to conjunctival test....	4— 3.8	100— 96
	Negative to cutaneous test.....	3— 3.8	75— 96
Doubtful.	Reacted to 1% conjunctival test.	4—11	33— 89
	Reacted to 5% conjunctival test.	3— 7	41— 13
	Reacted to the cutaneous test...	1— 6.7	125— 93
	Negative to conjunctival test....	9— 5	168— 95
	Negative to cutaneous test.....	7— 5.6	117— 94
Probable.	Reacted to 1% conjunctival test.	11—69	5— 31
	Reacted to 5% conjunctival test.	5—26	14— 74
	Reacted to the cutaneous test....	17—46	20— 54
	Negative to conjunctival test....	2—17	10— 83
	Negative to cutaneous test	1—10	9—90

Table II is arranged to show the relation of the tuberculin tests in patients becoming and those not subsequently becoming tuberculous. As our previous results have shown the 1 per cent conjunctival test is an important indication of active tuberculous disease and therefore, we look with most interest to the results derived from it. It will be seen that in the non-tuberculous group the four cases that later became tuberculous failed to react to the 1 per cent conjunctival test; whereas, the one case that did react has remained well. In the doubtful group of the 16 cases that subsequently became tuberculous only four originally showed a reaction to the 1 per cent conjunctival test. As far as the small number of cases collected can show anything, they indicate clearly that proportionately, the same number became tuberculous of those who reacted and of those who did not react to the tuberculin tests. We are therefore justified in concluding tentatively that the tuberculin tests are of value only in reference to the condition of the patient at the time they are given. Such a high grade of tuberculin hypersensitiveness as is indicated by a reaction to the 1 per cent conjunctival test is not to be used as

evidence of the presence of tuberculous disease when other clinical evidence is absent. A reaction to the 1 per cent conjunctival test, taken as an isolated fact, does not cast a gloomy shadow over the subsequent years of the reactor's life.

In the probable group, it will be noted, 69 per cent of those reacting to the 1 per cent conjunctival test became tuberculous, whereas but 23 per cent (the 5 per cent positive and the negative conjunctival cases combined) of those negative to the 1 per cent test became tuberculous. We have insisted that the patients in the probable group are really tuberculous and therefore these figures are further proof of the diagnostic value of the 1 per cent conjunctival test.

TABLE III.—THE AFTER HISTORY OF TUBERCULOUS PATIENTS IN RELATION TO THE TUBERCULIN TESTS.

		Well.	Advancing.	Dead.
Incipient.	Reacted to 1% conjunctival test.	7—58%	1— 8%	4— 33%
	Negative to 1% conjunctival test	6—66	3—33	0— 0
	Reacted to cutaneous test.....	9—64	2—14	3— 21
	Negative to cutaneous test	4—57	2—28	1— 14
Moderately advanced.	Reacted to 1% conjunctival test.	6—19	7—21	19— 60
	Negative to 1% conjunctival test	9—60	3—20	3— 20
	Reacted to cutaneous test.....	15—35	10—23	18— 42
	Negative to cutaneous test.....	0	0	4—100
Far advanced.	Reacted to 1% conjunctival test.	9— 9	6— 6	85— 85
	Negative to 1% conjunctival test	2— 4	4— 8	43— 86
	Reacted to cutaneous test.....	11— 9	6— 5	101— 85
	Negative to cutaneous test.....	0	4—13	27— 87

We have arranged Tables III and IV to give an answer to the question of the prognostic value of the tuberculin tests. In the incipient group, 33 per cent of those who reacted to the 1 per cent conjunctival test have died, while the six who failed to react are still living. In the moderately advanced group, a larger proportion have died of those reacting than of those failing to react to the 1 per cent conjunctival test. In the far advanced group the proportion between the two classes is practically the same.

TABLE IV.—COMPARISON OF LENGTH OF LIFE AND RESULT OF TUBERCULIN TESTS IN PATIENTS DYING OF PULMONARY TUBERCULOSIS.

		Death within 6 mos.	Death within 6 mos. to 1 yr.	Death within 1 yr. to 2 yrs.	Death over 2 yrs.
1% conjunctival test.	Positive ..	38—34%	34—30%	26—23%	14—12%
	Negative..	23—43	14—26	6—11	11—20
5% conjunctival test.	Positive...	8—42	7—37	1— 5	3—16
	Negative..	11—44	2— 8	4—16	8—32
Cutaneous test.	Positive ..	50—34	47—32	28—19	21—14
	Negative..	11—58	1— 5	3—16	4—21

Table IV indicates that in patients dying of tuberculosis, the length of life following the administration of the tuberculin tests is approximately the same in those who react as in those who do not react to the tuberculin tests.

We cannot discuss in detail the relation of tuberculin hypersensitiveness to tuberculous disease. We wish merely to call attention to the view that tuberculin hypersensitiveness is a measure of resistance to tuberculous disease. Certain important experiments upon animals have been interpreted as supporting the view and many prominent students of tuberculosis have subscribed to it. They hold that a tuberculous patient with a high grade of tuberculin hypersensitiveness offers a better prospect of recovery than one with mild or absent hypersensitiveness. Further, they regard attempts to diminish hypersensitiveness by tuberculin treatment as ill-advised. We have not shared these views. Our work with tuberculin in diagnosis and treatment has led us to believe that tuberculin hypersensitiveness in relation to tuberculous disease runs, roughly, somewhat as follows. Since nearly all adults are infected with tuberculosis, we assume a low grade of tuberculin hypersensitiveness to begin with. Should there be a fresh invasion of the body from within or from without, the tuberculin hypersensitiveness rapidly rises. If the disease subsides and the individual recovers the hypersensitiveness gradually falls to a lower level, perhaps to the original low level; if the disease remains active, the high level of hypersensitiveness persists and lasts until the body is overwhelmed and its resistance broken down completely by the disease when hypersensitiveness disappears. Therefore, while we allow that in rapidly advancing cases, the absence of tuberculin hypersensitiveness is an ominous sign, in early and moderately advanced cases, we consider a low grade of hypersensitiveness a more favorable indication than a high. The high level hypersensitiveness rebellious to tuberculin treatment we have found to be of particularly unfavorable prognostic import.

TABLE V.—RESULTS OF THE REPETITION OF THE CUTANEOUS AND CONJUNCTIVAL TESTS.

		Repeated in					
		Less than 1 yr.		1 to 2 yrs.		Over 2 yrs.	
		Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
1% conjunctival test.	Pos.	1	.....	.....	1	2	.....
	Neg.....	.....	.....	.....	5	12	35
5% conjunctival test.	Pos.....	.....	.....	.....	.....	2	4
	Neg.....	1	.....	3	1	9	24
Cutaneous test.	Pos.....	.....	.....	3	1	16	18
	Neg.....	.....	.....	2	1	12	19

Table V is arranged to show the results of the repetition of the conjunctival and cutaneous tests. As is well known, the application of tuberculin occasions a local stimulation of hypersensitiveness. A conjunctival test negative to one instillation may become violently positive if the instillation be repeated after a few weeks' interval. Our object was to see how long this local excitation persists. Of 50 patients negative to the 1 per cent conjunctival test, 12 were positive to a second instillation repeated from one to three years later. However, of these 12 cases four had in the interval become definitely tuberculous and five presented symptoms and signs pointing strongly to the presence of an active tuberculous lesion. Only three of the cases had remained unchanged in their general and local condition. It would appear, therefore, that the sensitiveness occasioned by a conjunctival instillation of tuberculin in most instances completely disappears within two years; in some individuals it may persist for two years and longer.

THE INFLUENCE OF THE CONTENTS OF THE PULMONARY ARTERY ON EXPERIMENTAL PULMONARY TUBERCULOSIS.*

By WM. CHARLES WHITE, M. D.,

WITH

A. MARION GAMMON and LESTER HOLLANDER, M. D.

(R. B. Mellon Research Laboratory of the Tuberculosis League of Pittsburgh, Pa.)

There are certain broad biological problems associated with pulmonary tuberculosis of the animal organism which have received surprisingly little attention in experimental laboratory work; yet these problems seem to me so fraught with importance that for two years our laboratory has devoted its whole time to their study.

So much of the investigation in tuberculosis during the past few years has been directed towards establishing a relation between this infection and the results of immunological studies in other infections, and especially the studies in anaphylaxis, that we have in a measure lost sight of some of the significant features of the disease that require elucidation before we have a foundation on which to build.

At the outset of this paper it may be well to state some of the unexplained anatomical facts which are evident to experimenters; to follow this with a review of some of the more prominent physiological processes connected with these conditions, and in conclusion to outline the methods of procedure attempted by us to clear away the difficulties; and finally to state the results of the work accomplished up to the present time.

In pulmonary tuberculosis in man and cattle there is undoubtedly a point of attack which is fairly constant. In man this is at the apex of the upper lobes; in cattle at the apical region of the caudal lobes. I think it may safely be said that this varying point of attack in the two animals is in some way connected with the posture of the animal, and probably with the fact that when the animal is on its feet the vessel which supplies the area usually infected in each case arises from the highest level of the blood stream. This fact opens the way for the constant operation of the law of gravity on the substances which form the component parts of the blood at the point of origin of these vessels from the parent stream.

If we examine the subject from this standpoint, it is pertinent to inquire first what substances are contributed to the blood stream in this region in such a way as to exert a possible influence by gravity or otherwise on a pulmonary infection.

It will be seen at a glance that the lung tissue gets first pick at a very striking contribution from various sources that no other organ in the body can boast:

1. The contents of the thoracic duct.
2. The contents of the hepatic veins.
3. The contents of the renal and suprarenal veins.

The substances contained in these vessels arrive from their various fields of production at the portals of the right side of the heart to receive a final churning here before being poured into the comparatively slow stream of the pulmonary artery, and from here spread out over the broad bed of the lung capillary system.

In calling special attention to these contributions to the blood stream, it is not intended to indicate that the contents of the blood from more distant regions have no bearing on this problem, but the above substances bear the stamp of grosser individuality and consequently have been chosen for the earlier studies.

The contents of these channels of contribution to the right heart require a more detailed account:

1. Through the thoracic duct there come chiefly large quantities of neutral fat in fine globules and granules, as well as cholesterin and lecithin, resulting from the action of bile, gastric, pancreatic, and intestinal secretions on the fats of the food.

2. Through the hepatic veins there come the blood sugar changed from glycogen by the action of diastase, the fats mobilized from the subcutaneous tissues and altered by the action of the liver and pancreatic secretions.

3. Through the renal veins the secretions of the kidneys and suprarenal bodies.

To arrive if possible at the influence of these various contributions to the pulmonary stream on tuberculosis infection in the lung, we outlined the following scheme of study:

THE INFLUENCE OF THE CONTENTS OF THE THORACIC DUCT.

1. Of various fats on the growth of the tubercle bacillus in vitro and on the tubercle bacillus in the lung.

2. Of the component parts of fat on the tubercle bacillus in the lung—

   (a) Glycerin and higher alcohols.
   (b) Fatty acids and soaps.

3. Of bile on the tubercle bacillus—

   (a) Before entrance to the lung.
   (b) Mixed with fats on the tubercle bacillus in the lung.

4. Of various salts, such as—

   (a) Phosphates.
   (b) Calcium.

5. Of various solutions which precipitate salts, such as—

   (a) Sodium citrate for calcium.

* Read at a meeting of The Laennec, a Society for the Study of Tuberculosis, The Johns Hopkins Hospital, March 31, 1913.

THE INFLUENCE OF THE CONTENTS OF THE HEPATIC VEINS.

1. Of liver altered animal fats—
   (a) On the growth of the tubercle bacillus in vitro.
   (b) On the tubercle bacillus growing in the lung.
2. Of liver and pancreatic secretion altered fat in vitro.
3. Of glucose—

Hyperglycemia	By glucose injection.
	By adrenalin injection.
	By pituitary extract injection.
	By thyroid extract injection.
Hypoglycemia	By injection of hydrazin.

4. Of surgical interference by—
   (a) Artificial stenosis of hepatic and pancreatic veins.
5. Of interference with liver function—
   (a) Phosphorus poisoning.
   (b) Starvation.

THE INFLUENCE OF RENAL AND SUPRARENAL SECRETIONS ON EXPERIMENTAL PULMONARY TUBERCULOSIS.

1. By the injection of renal extract intravenously.
2. By the injection of suprarenal extract intravenously.
3. By interference with kidney function by—
   (a) Phloridzin.
   (b) Other irritants.
4. By artificial stenosis of renal and suprarenal veins.

THE INFLUENCE OF VARIOUS DRUGS DIRECTLY APPLIED TO THE PULMONARY STREAM.

Fat solvents—ether, chloroform, benzol—
   (a) By inhalation.
   (b) Ether and chloroform intravenously.

It will be readily seen that such a scheme of study involves many years of work, and only parts of it have been accomplished up to the present time. In presenting what has been done I ask your tolerance of its incompleteness and the lack of positive conclusions which I am able to offer.

In the animal experiments in this series of observations, we have confined ourselves to rabbits and guinea-pigs. Rabbits are mostly used because of the ease of reaching the pulmonary stream through the ear vein.

We have used both bovine and human tubercle bacilli chiefly from the strains Bi and H_{37}, obtained from Saranac Lake through Dr. Baldwin.

EXPERIMENTAL PULMONARY INFECTION WITH TUBERCLE BACILLI.

Tubercle bacilli introduced into the animal body by various routes produce widely different distribution and grades of infection.

Subcutaneous injection produces a generalized tuberculosis, in which the liver usually escapes infection.

Intraperitoneal injection produces the most widespread generalized tuberculosis of all organs.

Gastro-intestinal introduction of tubercle bacilli is the most varying of all routes in its resulting infection. This route varies greatly with the animal used. Nearly all animals require very large doses to produce infection in this way. Especially is this true of guinea-pigs, which are so susceptible to the other routes of injection. Young pigs and monkeys are much more susceptible to this mode of infection. The resulting infection by this route is usually a glandular one, but may be pulmonary and generalized, depending largely on the dose.

By intravenous injection through the ear vein in rabbits, however, we are able to procure a more or less pure pulmonary infection with a varying slop-over infection of the kidneys and spleen.

LUNG CHEMISTRY.

I cannot do more than refer in this paper to certain striking phenomena of lung chemistry, such as the large lipase content and the specific character of the lung capillary endothelial cells and their affinity for tubercle bacilli, but these points must eventually be carefully studied and correlated with other results before the final conclusions of this infection are reached.

THE VIRULENCE AND DOSE OF THE TUBERCLE BACILLUS.

Such important factors as the virulence of the tubercle bacillus; the resistance of the animal to the dose of the bacilli; the disappearance of the tubercle bacilli from the blood stream; and similar factors have also a very striking bearing on this whole problem and cloud the experimental field more often than is generally appreciated. On no other grounds can I explain the varying results obtained in certain experiments carried out in one litter (the progeny of but two adults), in which individuals were found to yield strikingly different results to the same treatment.

In carrying out this work we have not forgotten the structure of the tubercle and its lack of blood supply, but we have thought that the chemical constitution of the region of tuberculous development in the lung as determined by its blood supply might have some fundamental bearing on the choice of a site by the tubercle bacillus.

I will now describe the results of our various experiments without wearying you with too great an amount of detail:

TEST TUBE EXPERIMENTS.

We found that various fats added to plain glycerin agar in the test tube had varying influence on the growth of the tubercle bacillus. Some fats markedly increased the growth; others prevented any growth.

The fats used in these experiments were—human fat, rabbit fat, beef fat, olive oil, palm oil, linseed oil, and cod liver oil. The fats were chosen largely on the basis of their content of the several fatty acid radicles—stearic, palmitic, oleic, linoleic, and linolic acids. They were examined for their influence on both bovine and human strains of tubercle bacillus.

Human fat, butter, and olive oil always stimulated the growth of the human bacillus.

Beef fat, olive oil, and linseed oil stimulated the growth of the bovine bacillus.

The other fats had a restraining influence on the growth of the organisms.

When extract of liver (dog, rabbit, and guinea-pig liver), prepared to conserve the lipase (Kastle), was added to the fats and incubated for two to three hours before adding them to the agar in the test tubes, all of the digested fats, except cod liver oil, stimulated the growth of both types of tubercle bacillus when compared with the growth on plain glycerin agar.

When the tubercle bacilli from these various fat tubes were injected into the ear veins of rabbits and into the peritoneal cavity of guinea-pigs in doses of 1 mgm., they were invariably more virulent than the tubercle bacillus grown on plain glycerin agar.

This was also true of the tubercle bacilli grown on the liver altered fat tubes.

In a series of similar experiments in which tubercle bacilli was grown on beef, rabbit, and butter fats, treated with dog liver extract plus dog spleen extract, the organisms were more virulent when tested on rabbits in the above way, but those grown on olive oil and cod liver oil were less virulent.

Influence of Various Oils Added to the Pulmonary Stream.

Series of rabbits were injected with 1 mgm. of bovine tubercle bacilli, grown on egg media, and treated by injecting various crude fats into the ear vein daily, every second day, and every third day, following the infecting dose.

The fats used were the same as in the test tube experiments —human fat, beef fat, olive oil, palm oil, cod liver oil, and linseed oil. The average dose of the fat was .25 cc.

The resulting infection in the rabbits treated in this way was always more severe than in the untreated rabbits. This was especially marked in those rabbits treated with olive oil, which we used in more experiments than the other fats on account of its fluidity.

In the olive oil treated rabbits, we found at times large cavities produced, which we have never found in hundreds of injections of untreated rabbits.

Lungs Stored with Various Fats.

We found that by injecting various fats into the ear vein that the lungs retained a large quantity of fat, producing in them a tough, oily consistency, with soapy feel and appearance. We consequently administered in several series of rabbits successive doses of the above fats, giving as high as seventeen doses of .25 cc. olive oil; seven doses of .25 cc. linseed oil, fresh unsalted butter, human fat and beef fat; and followed this with 1 mgm. of bovine tubercle bacilli. In all of these animals the resulting infection was much more severe than in the untreated rabbits. Rabbits vary greatly in the amount of fat that can be administered in this way—some animals died in convulsions with severe pulmonary congestion after the second and third doses. Others took as many as seventeen successive doses without symptoms of any sort.

Injections of Glycerin.

On the basis of the theory that fat taken in the food is broken up in the intestine into glycerin and fatty acids, we next tried the influence on pulmonary tuberculosis of adding glycerin in frequent doses to the pulmonary stream. We have not yet used any of the higher alcohols.

Glycerin is well known to be one of the valuable adjuncts in stimulating the growth of the tubercle bacilli on artificial media. As one of the essential components of fat, we tried the influence of glycerin on the development of tuberculosis in the lung by adding this alcohol to the pulmonary blood stream through the ear vein of rabbits.

Several series of rabbits, each series of one litter were injected with .5 mgm. of bovine tubercle bacillus through the ear vein. Commencing on the next day following the bacillary injection, all but one of these rabbits were treated by ear vein injections of .5 cc. of 25 per cent glycerin, one receiving 36 daily injections; one 20 similar injections every second day; and one 16 injections every third day. At the end of 40 days these animals were killed and compared with the untreated control.

In all of these experiments the treated animals lost weight more rapidly, and had much more extensive tuberculosis, the tuberculous processes being larger and more degenerated than in the untreated animals.

Similar series were injected with 3 mgm. of human tubercle bacillus and similarly treated. In these the glycerin injections had the same effect, the treated animals having more tuberculosis in size and number of the tubercles than the control animals.

Soaps of Fatty Acids and Fatty Acids.

In these experiments we have used only sodium oleate and oleic acid. Only the soap was tried on the pulmonary infection. In three series of rabbits which received .25 cc. of 1/10,000 solution of the soap, the treated rabbits all lost weight more rapidly than the controls, and had more severe and larger tuberculous lesions.

Oleic acid, besides its irritant action at the site of the injection, produced a very curious, soapy translucent condition in the lung, which we have not studied further.

Influence of Bile.

These experiments are still in progress. The indications, however, seem to be, from two series of animal experiments and many smears of tubercle bacilli mixed with rabbit bile and incubated for one to 24 hours, that the tubercle bacilli clumps are broken up, the resulting lesions more scattered, and the organisms less virulent.

Our impression from these experiments has been that we may find here an explanation of the difficulty of producing infection through the gastro-intestinal tract in most animals, and of the absence of pulmonary infection in man from the large numbers of bovine bacilli which he seems doomed to drink with his milk.

We have not yet touched the experiments on the influence of bile and pancreatic juice on fats in their relation to pulmonary infection; the experiments involving surgical interference; nor the influence of salts.

Calcium Precipitation by Sodium Citrate Solution.

Sodium citrate solution has the property of precipitating free calcium. With the idea of finding out if such a solution added to the pulmonary blood stream would aid the precipitation of calcium around tuberculous deposit on the possibility of free calcium joining the same stream through the thoracic duct, in conjunction with Dr. Lester Hollander, we injected rabbits with experimental pulmonary tuberculosis with increasing doses of sodium citrate solution from 1 mgm. up to 256 mgm. In rabbits living over two months there was extensive fibrosis with marked deposit of lime salts around the lesions both in the lungs and in the kidney.

In a series in which we injected sodium citrate solution and calcium lactate solution in opposite ear veins at the same time, the rabbits died immediately in convulsions.

Influence of Hepatic Vein Contents.

The experiments with liver altered fats have been confined to test tube experiments and have been referred to earlier in this paper.

Hyperglycemia.

The question of the influence of sugar on tuberculous infection of the animal body has long since held a conspicuous place as a clinical observation. So far as I know, the subject has not been made the object of experimental investigation from our standpoint. Nor has the question of relation of the two conditions, hyperglycemia and tuberculosis, kept pace with the rapid progress of our knowledge of diabetes. Recently Montgomery has made a careful analysis of the subject from a statistical and clinical standpoint, but in such studies the pathogenesis of the diabetes has not been taken into account, and it is evident that not all diabetic conditions have an equal relation to the tuberculosis process.

In approaching this subject we have had in mind the various forms of experimental diabetes, dependent on the chromaffin system; the pancreas; the ductless glands; the alimentary system; phloridzin; and Brown-Séquard's puncture, or the nervous system. On only three of these can we report at the present time:

1. On hyperglycemia caused by the injection of suprarenal extract, and thus producing an excessive sugar output on the part of the liver.

2. On hyperglycemia caused by adding glucose directly to the blood stream.

3. On diabetes caused by phloridzin, which does not carry with it a hyperglycemia, but probably causes its diabetes by its action on the kidney cells.

The pulmonary tuberculosis was produced in the ordinary way, by the injection of bovine tubercle bacilli into the ear vein of rabbits.

In several series of rabbits with pulmonary tuberculosis, treated with 1 cc. of 1/10,000 solution of suprarenal extract intraperitoneally and subcutaneously every second day for two months, the results were variable, but when there was any influence, it reduced the resulting infection.

One very interesting issue of this work was the different result on the kidneys and heart by subcutaneous and intraperitoneal injections.

After long continuous subcutaneous injections, the kidneys are astonishingly increased in volume—often to double the normal size.

After long continued intraperitoneal injections, the kidneys remain normal in size, but the heart becomes tremendously hypertrophied—to double the normal size in one instance.

Hyperglycemia from subcutaneous injections of glucose always increased the severity of the tuberculous infection.

Phloridzin diabetes apparently had no influence on the pulmonary infection.

By exclusion, it seems likely that if any of the hyperglycemias have a marked influence in increasing the severity of tuberculous infection, it is probably those due to the pancreatic system and the thyroid gland. This seems more likely from a clinical standpoint from the frequent enlargement of the thyroid gland accompanying tuberculosis infections.

Phosphorus Poisoning.

In using phosphorus poisoning to eliminate the influence of the liver on the content of the pulmonary stream, we are dealing with a complex alteration of metabolism. The general conclusions on the results of phosphorus poisoning in animals may be summed up as follows: The total metabolism is decreased; protein metabolism is increased; carbohydrate metabolism is probably increased; while fat metabolism is probably markedly decreased, leading to a decreased amount of fat and fat split products in the blood. In addition to this the alkalinity of the blood is diminished.

It will thus be seen that if phosphorus poisoning has any influence on experimental pulmonary tuberculosis, a process of eradication of the various component parts of such a condition would be necessary before any conclusions could be drawn.

We have so far studied the change in two series of rabbits.

In the first series of five rabbits, four were given pulmonary tuberculosis in the usual way—two of these were poisoned by phosphorus, receiving 1/25 grain daily for 4 days, and then 1/50 grain daily for eight days. They were killed at the end of 14 days and compared with one control. In the phosphor-

ized animals, which became emaciated very rapidly, the tuberculous processes were less than in the control.

The fifth rabbit was poisoned with phosphorus, 1/25 grain daily for four days before the injection of 1 mgm. of bovine tubercle bacilli, and after the dose of bacilli received 1/50 grain of phosphorus daily for 12 days. This was killed 19 days after infection and compared with rabbit No. 4, *i. e.*, the second control which had its infecting dose of tubercle bacilli four weeks before. This phosphorized animal also had less marked tuberculous processes than the untreated animal.

The second series consisted of four rabbits—all were given 1 mgm. of bovine tubercle bacilli through the ear vein; and three were phosphorized with 1/50 grain twice daily for four days, then once daily for four days, and were killed at the end of three weeks.

In the three phosphorized animals in this series, also, the tuberculous processes were less severe in size and number than in the untreated animal.

The phosphorus was administered by mouth in pill form; the livers of all animals were large, yellow, and fatty; the kidneys were yellow, soft and flabby.

The tubercles in all the phosphorized animals had a striking yellow tinge.

Any explanation of these results without further study would be useless, but the results may have something to do with a diminished amount of split fat products in the pulmonary stream.

STARVATION.

We have studied only one series of guinea-pigs so far to find the influence of starvation as a whole on the tuberculous process. This was entirely unsuccessful. Six pigs were given 3 mgm. of bovine tubercle bacilli by mouth, and three starved for four days, and then fed lightly for three weeks. The controls were given full diet. All the animals, save one of the unstarved, failed to develop tuberculosis, and this one had only a bronchial gland infection of mild degree.

RENAL VEIN INFLUENCE.

We cannot yet offer any data on this phase of the subject, save that given in the hyperglycemia studies above.

INFLUENCE OF FAT SOLVENTS BY INHALATION.

We have conducted experiments on many series of animals to find, if possible, if any of the ordinary fat solvents could be administered in such a way as to influence pulmonary tuberculous lesions.

ETHER AND CHLOROFORM.

These experiments have been conducted in several ways:

1. The lungs were saturated with ether and chloroform by inhalation for thirty minutes, and immediately following this, while the animals were still asleep, were given 0.1 mgm. of tubercle bacilli in the ear vein. They were allowed to live 44 days, when they were killed and compared with the controls. In the treated animals the tubercles in the lungs were less in number and much smaller than in the control, but the treated animals had more spleen and kidney lesions.

2. In several series, rabbits with pulmonary tuberculosis, produced by 0.1 or 1 mgm. of bovine tubercle bacilli, were etherized by inhalation with 15 to 25 cc. of ether daily for 20 to 30 minutes for as long as two months and ten days. We could not determine that such treatment had any constant influence on the pulmonary lesions when the animals so treated were compared with untreated controls. We were struck with the frequency with which we could etherize these animals without apparent influence on their general health. We could find neither glycosuria nor albuminuria in the etherized animals. If, however, they were exposed to cold air during the winter too soon after etherization, they frequently died of general pulmonary congestion.

BENZOL.

Animals with pulmonary tuberculosis (1 mgm.) allowed to inhale 2 cc. of benzol, under a glass cover, daily, every second day, and every third day, all showed less tuberculosis in size and number of tubercles than the untreated controls.

From these experiments, it is possible that ether and chloroform inhaled immediately before infection in rabbits may have some influence in reducing the amount of tuberculosis produced by tubercle bacilli introduced in the ear vein; that ether inhaled daily, or less frequently, for many days after such tuberculous infection has no influence on the pulmonary lesions; and that inhalation of benzol may have some restraining influence on the pulmonary lesion when administered after this has been produced.

I am sorry that this work is not nearer completion; also that the microscopic study of the gross experiments has not been touched up to the present time. When we have had time to complete it, we will, I hope, have something more to offer.

In recounting the nature and results of our experiments, we have refrained from explanation, preferring to confine ourselves at the present time to the facts only. I feel, however, that it is fair to conclude:

1. There is some close relation between the content of the fats and split fat substances in the pulmonary stream and the severity of experimental pulmonary tuberculous lesions.

2. That increasing the percentage of carbohydrate content of the pulmonary stream by the influence of extracts of the suprarenal gland, has no influence on experimental pulmonary tuberculosis.

3. That the inhalation of such fat solvents as ether, continued over long periods of time, has no direct influence on experimental pulmonary tuberculosis.

THE PHYSICIAN'S OPPORTUNITY IN PREVENTIVE MEDICINE.*

By John B. Hawes, 2d, M. D., Boston, Mass.

Prevention is to-day the watchword of medicine. At the present time no physician who attempts merely to cure disease and not to prevent it can be said to be doing his duty toward the community. In tuberculosis as in all other conditions new methods of treatment are constantly being discovered. A few prove of great and lasting service; the majority do not. In the meantime, often without pay, usually without adequate pay or reward there are many physicians engaged in preventive work which will eventually place tuberculosis and other similar diseases under our control. I refer to the physicians occupying public positions whose aim it is to prevent disease rather than to cure it. They are the family physicians not of sick individuals, but of sick communities. In this paper I shall describe what these men are doing in my own state, what they have done and what they hope to do, the handicaps under which they work, and the rewards, financial and otherwise, which they receive. I shall try to give a clear picture of the difficulties and disappointments which one meets with in this work, as well as to present the other side, the vast opportunity open to men, and particularly young men, trained in one of the best, I will not say the best, medical schools in the world to be of service to city, state and country.

My own position in Massachusetts is a particularly advantageous one from which to view the field, in that I am not only a health officer in the employ of the state, but also a general practitioner in the city of Boston, especially interested in tuberculosis. It was far from my original plan to go into state work. I had fully expected to enter the field of general medicine and through my good fortune in becoming the assistant of Dr. F. C. Shattuck I had every reason to continue along the smooth roadway of the private practitioner. In 1907, the late Dr. Arthur T. Cabot, newly appointed chairman of the State Tuberculosis Commission, asked me to act as secretary to the board. As this position not only drew a salary which seemed to me large but also permitted of my continuing my work with Dr. Shattuck, my own private practice, such as it was, and my work at the Massachusetts General Hospital, I gladly accepted Dr. Cabot's offer. This position with constantly increasing duties and responsibilities I have held ever since.

At first I felt very strongly that many of my medical friends, particularly the older ones, not only for my own sake thoroughly disapproved of my taking up any state work, however minor a position it might be, but also that they looked askance at those who left the straight and narrow path of surgery, internal medicine or the laboratory bench. Doubtless many of these physicians would vigorously deny that they ever felt in this way. Every public health officer, however, who, during the last ten years has been actively at work, will agree with me that this feeling was not an uncommon one. During the past two or three years, in Massachusetts at least, there has come a very remarkable change in the attitude of the medical profession toward the doctor in public office. The development of preventive medicine has brought this about. Doctors are coming to realize that while in their general practice or limited specialty they may cure this or that individual patient, disease as a whole, and the mass of the people as a whole, cannot be reached in this way. They have come to respect and not to look down upon the men who are in public service. The public is realizing that protection from tuberculosis, typhoid fever and infantile paralysis does not come from the private practitioner, no matter how great his skill, but that it depends on municipal and state efforts wisely directed by physicians trained and devoting their lives to this work.

I crave your indulgence for what I have said concerning my own start in this field. My excuse is that I believe my experience has been an instructive but not uncommon one; that it represents a condition of affairs now relegated to the past and that the attitude of the medical profession to-day toward the physician in public service is in happy contrast to what it was even only six years ago. With this introduction I shall now consider, in as practical a manner as possible, the various positions open to physicians in which they can be of service to the community in which they live. Conditions in Massachusetts to a greater or less extent find their counterpart in other states.

Such positions naturally divide themselves into two classes, those that are paid and those that are unpaid. The former list includes town and city physicians, school and factory inspectors, positions on local boards of health, officers of state boards of health and other state boards, superintendents or assistant superintendents and physicians in state or local tuberculosis sanatoria, hospitals and other institutions, and finally, positions in the state legislature. Unpaid positions include the officers of state and county medical societies, positions of trust in local anti-tuberculosis associations, members of unpaid boards of trustees of local or state institutions, members of unpaid state commissions and members of local or state boards of health.

Town or City Physicians.—In smaller cities, and in practically all towns, there is always some position which corresponds to what in Massachusetts is called the city physician. Too often this office is under political control and is handed out as a reward of merit. The physician can usually carry on private practice of his own, and can do the city work at his own convenience. His work is under the supervision of the local board of health; it consists in caring for indigent cases either in their homes or in institutions, and especially in investigating contagious cases reported to the board. The salary runs from $500 to $2000. Whether this position is or

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is not held in respect and esteem by the medical profession and by the public at large depends upon the caliber of the incumbent. I know of several physicians holding such positions, who I am sure are doing splendid work, especially in tuberculosis; I also know of others who are not. The position is an honorable one and one in which a high-grade man could be of immense benefit to his community.

City Bacteriologists.—The salary of a city bacteriologist runs from $500 to $2000 depending on the amount of time given to the work. Except in the cases of large cities where this is a department of the board of health and where there may be a number of physicians giving their whole time to the work, a city bacteriologist can carry on his own private practice giving one to four hours a day to the laboratory.

Milk Inspection, Etc.—There are often other minor paid positions, such as inspectors of milk, water supply, etc., under local boards of health. Too often they are under political influence and rarely occupied by high grade men. The salaries are small.

Local Boards of Health.—A local board of health may be an admirable institution or it may be a school for turning out cheap politicians. Too often, in Massachusetts at least, local boards seem to be of the latter type. In many of the smaller towns there is no medical man on the local board, or, indeed, there may be no health board of any kind, the selectmen acting as such. As a general rule, the best physicians have no opportunity and make no attempt to secure positions on such boards, nor does the public yet demand that the medical profession have adequate representation on them. The tenure of office is only a temporary one and the salaries are not large, $100 in smaller towns, to $1000 in cities; they are large enough to attract non-medical office hunters but not enough to secure the services of the best physicians. Local boards of health, however, are slowly improving. The time is not far distant when a strong public opinion will not tolerate political influences in the administration of its health affairs. Opportunities for young men, fairly good now, are bound to become better. There is no greater opportunity than this for the highly trained young physician, not only to raise the standard of health work in his community to a height never before dreamed of, but also to gain for himself name and fame, which will bring their own reward.

School Inspection.—There is hardly any subject in medicine concerning which more is being written and more accomplished than school hygiene. Proper school inspection is a necessary and integral part of such school hygiene. Until comparatively recently in smaller cities or towns, either there was no school inspection or else it was done in a purely perfunctory way, the most important part of the physician's duty being to draw his salary. This is rarely the case at present. The public fully realizes the value of fresh air rooms, open air schools, and that it is better to keep the child well than to wait until he gets sick before placing him under proper conditions at home and at school. The standard demanded in this work is constantly rising; unfortunately, the salaries have not yet risen in proportion. In the city of Boston there are 87 school inspectors, civil service appointees, under the supervision of Dr. W. J. Gallivan, chief of the division of child hygiene. These physicians are paid $500 to $1000 a year and are required to give two hours daily to the children under their care. There is also a large corps of school nurses working in conjunction with these doctors. While the present system is by no means a perfect one, it is immensely superior to anything in this line Boston has heretofore enjoyed. It is the desire of the chief of this department, and indeed of all those interested in the subject, that the amount of time required of each physician and the salary paid him be steadily raised. In smaller cities and towns the salary of the school physician is much less and his duties much less clearly defined; as a general thing, the quality of the work is proportionately low. It rests solely with the individual physician whether such school inspection be purely perfunctory or whether it really amounts to something. One school inspector, a busy man in general practice, in addition to his stated duties, has arranged for a series of short health talks to be given by specialists to the high school pupils under his care. These talks include such subjects as hygiene, tuberculosis and its prevention, the care of the teeth, etc. I spoke to such an audience of over 1000 bright and intelligent pupils the other day and was glad of the opportunity to do so. This kind of "school inspection" is preventive medicine on a large scale. This position, wherever it may be, is one of great and growing importance; the physician who undertakes this work, regardless of inadequate remuneration, and who does it conscientiously and intelligently, will soon gain an enviable place for himself in his community wherever that may be.

Welfare Work in Factories, Workshops, Department Stores and Large Corporations.—There is a steadily growing feeling among manufacturers and other large employers of labor that from the financial point of view alone it is more profitable to keep their employees well than to allow them to get sick and try to care for them after they become sick. The really progressive employers try to do both. They are learning that healthful conditions are an asset in their business. This necessitates the help of doctors and nurses. Such positions as these are admirable ones for younger physicians. Not only is the salary usually paid a good one, $1000 to $1500 or over, while in addition the range of medical and surgical cases is wide and varied, but also such a position often gives the physician holding it his first practical example of the meaning of the words "preventive medicine." I have been through the workshops and addressed the employees of the Dennison Manufacturing Company, which admirable concern employs a physician and a nurse, each of the highest standing, to look after the welfare of the men and women in the factory. Never have I seen more hygienic workrooms nor a healthier and more contented group of employees. Such positions as the one here described are rapidly increasing in number. A man undertaking this work will at once find opportunities to prevent disease and to become a factor in the health of his community, which he probably would not have met until after many years of general practice and perhaps never.

State Health Work. State Board of Health.—In Massachusetts the position of secretary and the assistant to the secretary of the State Board of Health command good salaries and are at present occupied by physicians of high standing, who give all of their time to the work. Massachusetts has so far been fortunate in that these important positions have been kept out of politics, and in consequence are sought after by men of good training and ability. Those who hold these positions are, in general, looked up to and respected by the medical profession and the community at large. The salaries are from $3000 to $5000.

State Inspectors of Health.—The position of state inspector of health is a comparatively new one in this state and in many other states does not exist at all. Our health inspectors are appointed by the governor each year; they are not yet under civil service. The salary paid varies from $1200 to $2500 per year depending on the size and population of the individual district. The state is divided off into fourteen health districts. Among his other duties the health inspector in charge of a given district, acting under the supervision of the State Board, is supposed to see that laws in regard to factory and workshop hygiene are enforced, to carry out investigations of epidemics or of special diseases as directed by the State Board, and to advise local boards of health and direct their work when necessary. One most important duty of health inspectors is to examine into the health of all minors employed in factories, and to inspect the sanitation of factories, workships and tenement houses where clothing is made. One inspector in one year examined as a part of his work the sanitary conditions of 342 factories of 63 different industries employing 31,000 hands, of whom 3,800 were minors. Another inspector has made a special study of a number of trades in which workers are exposed to dusts, to irritating and poisonous fumes, to extreme degrees of temperature and humidity. The industries so far studied include the textile industry, the pearl industry, felt hat industry, mattress and curled hair industry, the rubber industry, the making of jewelry, metal polishing and buffing, and a group of industries in which workers are exposed to lead poisoning. Although it was understood at the beginning that this work need not interfere with nor prevent the carrying on of general practice by the physicians accepting these appointments there is no doubt but that it has seriously interfered with the practice of many of the inspectors and that in many ways they have to curtail their private work. This at best is unsatisfactory. The work is large enough to demand the full time and energy of a highly trained physician; the salary should be large enough to permit of this. However, this may be, these positions offer splendid opportunities for the highest kind of service. At present there is no adequate financial reward; in the future, and I believe in the near future, the public will see the value and need of this work and will demand that these positions be multiplied and the salaries increased.

There are numerous other salaried positions under any well organized state board of health. These are usually full time appointments and do not allow of private practice. Among such positions one might name those of bacteriologists, inspectors of cold storage plants, physicians engaged in making special investigations, etc.

Secretaryships of State Commissions.—My own position is an example of this type. The work I do fits in excellently with that of my private practice and each helps and augments the scope of the other. Such work throws one into contact with problems of all kinds, and doctors and patients of every description, and most important of all gives one a clear perspective of the big administrative side of preventive medicine, which can rarely be gained from private practice. The salaries usually paid in such positions which permit of private practice vary from $1500 to $2500.

Superintendents and Resident Physicians of State, Municipal or Private Tuberculosis Sanatoria, Hospitals or Other Institutions.—In Massachusetts, as elsewhere in the east at least, there is a dearth of good men who are willing to take up institutional work. The reasons for this are plain. The deadly routine, comparative isolation, and on the whole low scale of salaries are sufficient to lead most men to prefer to take their chances at private practice. This is the state of affairs at present. I do not believe that it will last long. Public opinion will demand that men of the highest and best type be obtained for these positions and that such men need make no sacrifice, as many of them now do, to take up this form of medicine. In our state sanatoria the superintendent receives $2500 salary and a comfortable home for himself and his family; assistant superintendents get from $900, the lowest, up to $1800, the highest, with, but more often without, accommodations for wife and family. Personally I believe that these salaries should be raised 25 to 50 per cent; in a few years I feel sure that they will be so raised. But even as they are, these positions offer opportunities for young men to support themselves and get the best of training along certain lines during their earlier years of practice, as well as opportunities to do yeoman's service in preventive medicine. What I have said here in regard to our tuberculosis sanatoria applies equally well to the many other similar positions in hospitals for acute or chronic diseases or in institutions for the criminal or the insane.

Positions in the Legislature. In Massachusetts, as well as in other states, there are always a few physicians in the Senate or House of Representatives. Occasionally the doctors holding such offices are of the highest type; as a general rule, in Massachusetts at least, they are good average men; not infrequently they are purely politicians. I believe that in Massachusetts such physicians at the State House are conscientious and sincere in their desire to do good. They are, however, usually untrained for such work; they rarely have had any previous opportunity to look at medicine from a broad, administrative point of view; they are not forceful in debate or public speaking and their influence for good is apt to be lost in the mælstrom of political give and take. Again, they are rarely helped as they should be, or backed up by the state medical society which is only too apt to take no active part in legislative affairs. The opportunity to do much good in this

direction is ever present. I could not advise any physician to enter the field, however, unless he was fully trained to this work, willing and able to devote to it not one year but many years, and unhampered by the thought of a neglected private practice.

Other Salaried Positions.—There are many other salaried positions the details of which I will not go into but will merely enumerate. Various state boards such as the Board of Charity, or its equivalent, the Board of Insanity, state water boards and civil service and industrial commissions, offer positions drawing good salaries to physicians trained along certain lines. Various philanthropic societies such as those connected with baby hygiene, mental hygiene, milk bureaus, tuberculosis, eugenics, vital statistics, etc., employ physicians, most of whom are able to carry on private practice in addition.

In the preceding pages I have gone over the chief salaried positions open to physicians, particularly the younger men. I shall now consider what I call the higher positions, whose chief reward, in addition to some increase of reputation of uncertain value, is the feeling that one is helping to accomplish good work and to bring about real progress.

Local Anti-Tuberculosis Societies.—Beginning with the smaller local positions, I would at first call attention to those connected with local anti-tuberculosis societies. During the last ten years in Massachusetts, I have seen the number of such local societies increase and multiply until now every city and every large town has an organization of some kind doing anti-tuberculosis work. No one can really estimate the amount of good these societies have done. I can, however, name off a long list of local day camps, municipal and private tuberculosis hospitals and sanatoria, out door schools, dispensaries and district nursing associations, whose existence has been brought about entirely by the influence of these local societies. But, back of the local societies, I can also name a long list of men, young doctors and old doctors, and all busy doctors, each one dependent on his practice for his living, who have given freely of their time, influence, wisdom and energy to bring about what I have described. To you, in Baltimore, the names of J. F. A. Adams of Pittsfield, Bowers of Clinton, Getchell of Worcester, Alfred Worcester of Waltham, and many others, may possibly mean but little; to us in Massachusetts they mean men who have stepped out of the rut of private practice, often to the detriment of their private practice, to be real leaders in the fight to prevent disease. To them the state owes a debt it can never adequately pay.

County Medical Societies.—The chairmanships of county medical societies are few in number and usually bestowed as a reward of merit. Too often the man holding such a position regards it in exactly this way and does not exert himself to make what should be made of it. The chairman should do more than simply preside, but most of them do not. He can be a great influence for good in his medical community by leading in new movements, formulating plans, and by helping to direct public opinion providing he has courage and inclination to do this.

Boards of Trustees of State or Local Institutions. State Commissions.—Massachusetts still holds to the system of managing most of the state institutions by means of unpaid boards of trustees; many of the biggest pieces of preliminary survey work which have led the way to the establishment of new hospitals and sanatoria, or to the enactment of beneficent legislation, have been done by such unpaid boards and commissions. Such work is arduous; it takes much time; it often meets with the severest and most unjust criticism. The men carrying it on are known as such and such a board, and rarely as individuals. It takes real public spirit and real patriotism for the busy physician striving his best to earn his living and often having hard work to do it, to accept such a position and give it the necessary time, energy and thought. His only reward will be the increased esteem of those members of the medical profession, the value of whose good opinion cannot be measured in dollars and cents.

Training in Preventive Medicine.— Up to the present time men occupying any of the positions, paid or unpaid, which I have enumerated above, have had practically no special training to fit them for the work they were called upon to do. The reason for this was that there was no opportunity for such training. A physician accepting a public service position usually entered upon his work with absolutely no previous experience of any kind; he felt his way along, making many and sometimes serious blunders; but, if wise and conscientious, profited by them until he became an able and competent health officer.

This state of affairs no longer exists. The medical profession and the public alike demand that the men in charge of health matters must be highly trained and specialists in their work. At the Harvard Medical School, and at other schools, there is a department of preventive medicine which is constantly growing in its influence and scope. This department, under the charge of Dr. Milton J. Rosenau, offers the degree of Doctor of Public Health to those completing the course. The demand for physicians who have taken this course and received this degree of D. P. H. is constantly increasing and will soon exceed the supply. I am assured that during the past six months at the Harvard Medical School, there have been more than six requests for men well trained in public health work, at salaries varying from $2400 to $7000 a year. In addition to this, the department is now about to offer another and shorter course open to graduates, which will provide a splendid opportunity for physicians about to take up some form of health work, who cannot spare the time necessary to acquire the full degree of Doctor of Public Health. This new course, in addition to other things, will include actual field work under the supervision of the State Board of Health and other agencies.

It is evident, then, that in the not far distant future the doctor who intends to take up preventive medicine must regard it as a specialty and a most exacting one, requiring special study and training. Success in this branch, as in other branches of medicine, can only come by devoting one's entire time to the work, and not only time but heart and

soul. Ten years from now it will be difficult to combine private practice with public health work. The general feeling of the community is gradually reaching the point where it sees that the training of the ordinary doctor does not fit him to be a sanitarian. There is no excuse, even at the present time, for any medical student not securing the best possible training for public health positions.

Meanwhile, until the time arrives when adequate salaries are paid to public health officers, so that no financial sacrifice need be made by those entering this field, many physicians will have to combine private practice with whatever public office they may hold. Except in the larger cities it may be many years before this millennium arrives. That it is coming there can be no doubt. The next generation of doctors will find a condition of affairs in this regard far different from what now exists. This, however, does not lessen the responsibility of the doctors of to-day, and especially the younger doctors, toward preventive medicine. The conditions which I have described above are not peculiar to Massachusetts. They exist everywhere. It is far easier to stick to private practice or to develop some specialty, than to endure the criticism and disappointment often met with even in the humblest of public positions. But nowhere in private practice can be found such opportunities to prevent disease and to be of real service to the community as are ever present in each of the positions above described.

There are two men, familiar to you all, whose names will be handed down in the history of Massachusetts and of preventive medicine in this country. The first is Dr. Henry P. Walcott, chairman of the Massachusetts State Board of Health, who, without remuneration, for over a quarter of a century has been the acknowledged leader in the fight to protect the health of Massachusetts citizens and to eradicate disease from their midst. I need not mention his further service to the state through his connection with Harvard University and the Massachusetts General Hospital. Criticism, disappointment, even slander and abuse, have never let him swerve from his lofty aims. He has been a true physician to the state.

The other name that I would mention is that of Dr. Arthur Tracy Cabot, who died November 4, 1912. Six years ago Governor Guild appointed Dr. Cabot member of an unpaid state commission given wide powers to direct and control the tuberculosis campaign in this state. Dr. Cabot was at once elected chairman of this board, which position he held up to the time of his death. Despite the fact that he was a surgeon of national reputation, an acknowledged leader in his specialty, and had a large and lucrative private practice, he accepted this position and the duties and responsibilities which went with it. Shortly after this, he gave up his practice and devoted all of his time and energy to the service of the state. The future alone will show the true worth of these services; even at present, however, his influence is plainly evident. I know of no finer monument than that which has been erected to Dr. Cabot. When he took hold of the tuberculosis work in this state, there was little of order and system, and much of chaos in our methods. The state was in urgent need of a master mind and firm guiding hand to direct and lead the scattered forces. Such a mind and guiding hand Dr. Cabot gave at immense personal sacrifice. He has directed the building of three new state sanatoria; he has seen local hospitals for advanced consumptives increase and the death rate from this disease diminish; he has been influential in placing school and factory hygiene upon a proper basis; he has united the medical profession and developed among the public a deep-rooted conviction that tuberculosis can and must be eradicated.

We cannot all hope to accomplish as much as these two men have done, but, at least, we can do our share. I have tried in the limited scope of this paper to point out in a practical way the opportunities for such work as this. As I have shown, rarely is the financial reward adequate to the time and labor expended; but there are many things more worth while than rewards in dollars and cents. There is a sense of satisfaction that is well worth having in feeling that one is playing a part, however minor a part, in work which aims not only at the good of the individual but of the community. In addition to this, if I read the signs of the times aright, this is to be the medicine of the future. It seems to me, then that it is our very urgent duty, not only as physicians but also as citizens, to be ready and willing to do our share, to step aside from the routine of private practice and to take part in this world-wide effort not only to cure but to prevent disease.

ARMY MEDICAL CORPS EXAMINATIONS.

The Surgeon General of the Army announces that preliminary examinations for appointment of First Lieutenants in the Army Medical Corps will be held on July 14, 1913, at points to be hereafter designated.

Full information concerning these examinations can be procured upon application to the "Surgeon General, U. S. Army, Washington, D. C." The essential requirements to secure an invitation are that the applicant shall be a citizen of the United States, shall be between 22 and 30 years of age, a graduate of a medical school legally authorized to confer the degree of Doctor of Medicine, shall be of good moral character and habits, and shall have had at least one year's hospital training as an interne, after graduation. The examinations will be held simultaneously throughout the country at points where boards can be convened. Due consideration will be given to localities from which applications are received, in order to lessen the travelling expenses of applicants as much as possible.

In order to perfect all necessary arrangements for the examination, applications must be completed and in possession of the Adjutant General at least three weeks before the date of examination. Early attention is therefore enjoined upon all intending applicants. There are at present forty vacancies in the Medical Corps of the Army.

NEW PUBLICATIONS.

The following three monographs:

Free Thrombi and Ball-Thrombi in the Heart. By J. H. HEWITT, M. D. Price, $1.00.

Benzol as a Leucotoxin. By LAURENCE SELLING, M. D. Price, $1.00.

Primary Carcinoma of the Liver. By M. C. WINTERNITZ, M. D. Price, 75 cents.

are now on sale by THE JOHNS HOPKINS PRESS, Baltimore. Other monographs will appear from time to time.

NOTES ON NEW BOOKS.

The International Medical Annual. A Year Book of Treatment and Practitioners' Index. Thirty-first year. $3.50. (*New York: E. B. Treat & Company, 1913.*)

Carefully prepared as it is by leading English and American specialists, this Annual is an excellent review of the progress of medicine during the past year. No such work can satisfy all demands, but for the general practitioner it is a most useful volume. Some reviews do not seem to be up to date—*ex.*, the diseases of the pituitary body, where there is no reference to Cushing's work, and the writer appears not to know that the gland has been operated upon successfully in a number of patients. The volume is well illustrated, is of convenient size and neatly printed.

Handbook of Diseases of the Rectum. By LOUIS J. HIRSCHMAN, M. D. Second Edition Revised and Rewritten. (*St. Louis: C. V. Mosby Company, 1913.*)

This book appears as a second edition and has been revised and rewritten. The chief improvements made have been in the illustrations of the book, and in the attention devoted to local anesthesia. The illustrations are particularly good and constitute perhaps the most valuable feature of the entire work, including four colored plates and numerous prints from radiographs. Besides the body of the book which Hirschman himself has written there are incorporated two chapters by other authors. Dr. John L. Jelks of Memphis, Tenn., has written the chapter on dysentery and Dr. George W. Wagner of Detroit, is the author of a chapter on the examination of the feces. As a whole the book strikes one as being unoriginal, and not particularly needed.

The volume is expressly designed to serve the general practitioner, and hence contains no description of the larger operative procedures in this field of work. There is, however, extensive consideration of the operations which may be done under local anesthesia, and this feature of the book is its best claim to being worth while. The general arrangement and contents of this volume differ in no important way from the numerous other books on the same subject, and except that the material is perhaps more readable and condensed the reviewer finds no special worthiness in the volume now under consideration.

Lang's German-English Dictionary of Terms Used in Medicine and the Allied Sciences. Second Edition Edited and Revised by MILTON K. MEYERS, M. D. $5. (*Philadelphia: P. Blakiston's Son & Co., 1913.*)

There are but few medical students who read German with ease, and this well printed dictionary will be a real boon to them. It is not too large to be readily and frequently turned to, and with its nearly 50,000 words will very seldom fail to give the reader what he wants. It would be an incalculable help to the profession if there were similar dictionaries in other foreign languages, as good as this one.

Appendicitis—Its Diagnosis and Treatment. By JOHN B. DEAVER, M. D., etc. Fourth Edition Thoroughly Revised. $4. (*Philadelphia: P. Blakiston's Son & Co.*)

Appendicitis, both acute and chronic, is one of the commonest affections the surgeon meets with, and he could have no better book than this on which to found his surgical procedure. This last edition shows many changes since the third appeared. The excellence of Dr. Deaver's work has been recognized long since, so that this volume needs no new word of appreciation, except to mark it as the most authoritative work on the subject in English.

Organic and Functional Nervous Diseases. A Text-book of Neurology. By M. Allen Stan, M. D., etc. Fourth Edition, Thoroughly Revised. Illustrated. (*New York and Philadelphia: Lea & Febiger, 1913.*)

The many excellencies of this text-book have been known for years to neurologists and general practitioners, and it is fortunate for the profession that Dr. Stan has found time to prepare this new edition, which contains all that is essential in the newer studies of neurological diseases, that has appeared since the preceding edition. It is a work in every sense well adapted to the needs of medical students, and one which holds a foremost rank among American books of medicine.

Principles of Hygiene, a Practical Manual for Students, Physicians and Health Officers. By D. H. BERGEY, M. D., Fourth Edition. Illustrated. $3. (*Philadelphia and London: W. B. Saunders & Co., 1912.*)

We have already had the opportunity of commenting favorably upon previous editions of Bergey's text-book of hygiene, and take pleasure in referring to the fourth edition which has recently appeared. This edition is considerably larger than previous ones, and includes many of the most important advances which have been made in hygiene during the past few years. The section on quarantine is particularly good, giving in detail the quarantine laws in the United States in regard to shipping from foreign countries, and those governing interstate commerce. It is unfortunate that the author has not given in greater detail the various methods which are employed in hygiene especially since most students employ a book of this character as a guide to laboratory work. The book is full of information, however, is written in simple English, is essentially readable and can be heartily recommended.

BOOKS RECEIVED.

American Association for Study and Prevention of Infant Mortality. Transactions of the Third Annual Meeting, Cleveland, Ohio, 1912. 8vo. 383 pages. 1913. The Franklin Printing Co., Baltimore.

Bovine Tuberculosis and Its Control. By Veranus Alva Moore, B. S., M. D., V. M. D. Thirty full page illustrations. 1913. 8vo. 134 pages. Carpenter & Company, Ithaca, N. Y.

Annual Report of the Surgeon General of the Public Health Service of the United States. For the fiscal year, 1912. 1913. 8vo. 261 pages. Government Printing Office, Washington.

Year-Book of the Royal Society of London. 1913. 8vo. 258 pages. Harrison and Sons, London.

Eighth Biennial Report of the Board of Control of State Institutions of Iowa. For the Biennial Period ending June 30, 1912. 1912. 8vo. 736 pages. Emory H. English, Des Moines.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. Edited by Henry W. Cattell, A. M., M. D. Volume I. Twenty-third Series. 1913. 8vo. 302 pages. J. B. Lippincott Company, Philadelphia and London.

Systematic Case-Taking. A Practical Guide to the Examination and Recording of Medical Cases. By Henry Lawrence McKisack, M. D., M. R. C. P., Lond. 1913. 12mo. 166 pages. Paul B. Hoeber, New York.

Surgery. Its Principles and Practice. By Various Authors. Edited by William Williams Keen, M. D., LL. D. Volume VI. With 519 illustrations, 22 of them in colors. 1913 8vo. 1177 pages. W. B. Saunders Company, Philadelphia and London.

Solidified Carbon-Dioxide. In the Successful Treatment of Cutaneous Neoplasms and other Skin Diseases, with Special Reference to Angioma, Epithelioma and Lupus Erythematosus. Fully illustrated. By Ralph Bernstein, M. D. 1912. 12mo. 95 pages. Frank S. Betz Co., Hammond, Ind.

Scientific Memoirs. (*New Series.*) By Officers of the Medical and Sanitary Departments of the Government of India. Superintendent Government Printing, Calcutta, India.

No. 57. Studies on the Flagellates of the Genera Herpetomonas Crithidia and Rhynchoidomonas. No. 1. The Morphology and Life History of Herpetomonas culicis, Novy, MacNeal and Torrey. By Captain W. S. Patton, M. B., I. M. S., 1912. 4to. 21 pages.

No. 58. Studies on the Mouth Parts and Sucking Apparatus of the Blood-Sucking Diptera. No. 2. Some Observations on the Morphology and Mechanism of the Parts in the Orthorapha. By Captain F. W. Cragg, M. B., I. M. S. 1913. 4to. 33 pages.

No. 59. Studies on the Mouth Parts and Sucking Apparatus of the Blood-Sucking Diptera. No. 3. Lyperosia minuta Bezzi. By Captain F. W. Cragg, M. B., I. M. S. 1913. 4to. 36 pages.

Nervous and Mental Disease Monograph Series. No. 17. Freud's Theories of the Neuroses. By Dr. Eduard Hitschmann. Authorized translation by Dr. C. R. Payne. With an Introduction by Ernest Jones, M. D., M. R. C. P. 1913. 8vo. 154 pages. The Journal of Nervous and Mental Disease Publishing Company, New York.

Saint Bartholomew's Hospital Reports. Edited by H. Morley Fletcher, M. D., and W. McAdam Eccles, M. S., F. R. C. S. Vol. XLVIII. 1913. 8vo. 187 pages. Smith, Elder & Co., London.

Transactions of the College of Physicians of Philadelphia. Third Series. Volume the thirty-fourth. 1912. 8vo. 450 pages. Printed for the College, Philadelphia.

Diabetes: Its Pathological Physiology. By John J. R. MacLeod, M. B., Ch. B., D. P. H. International Medical Monographs. General Editors, Leonard Hill, M. B., F. R. S. and William Bulloch, M. D. [1913.] 8vo. 224 pages. Longmans, Green, and Co., New York; Edward Arnold, London.

International Medical Annual. A Year-Book of Treatment and Practitioners' Index. Thirty-first year. 1913. 8vo. 628 pages. E. B. Treat & Company, New York.

The Interpretation of Dreams. By Prof. Dr. Sigmund Freud, LL. D. Authorized translation of third edition with introduction by A. A. Brill, Ph. B., M. D. 1913. 8vo. 510 pages. The Macmillan Company, New York.

Clinical Laboratory Methods. A Manual of Technique and Morphology Designed for the Use of Students and Practitioners of Medicine. By Roger Sylvester Morris, A. B., M. D. 1913. 8vo. 343 pages. D. Appleton and Company, New York & London.

Epidemic Cerebrospinal Meningitis. By Abraham Sophian, M. D. Twenty-three illustrations. 1913. 8vo. 272 pages. C. V. Mosby Company, St. Louis.

Private Duty Nursing. By Katharine De Witt, R. N. 1913. 12mo. 244 pages. J. B. Lippincott Company. Philadelphia & London.

Tuberculin in Diagnosis and Treatment. By Francis Marion Pottenger, A. M., M. D., LL. D. With thirty-five illustrations, including one plate in colors. 1913. 8vo. 243 pages. C. V. Mosby Company, St. Louis.

Lang's German-English Dictionary. Of Terms Used in Medicine and the Allied Sciences. Second edition edited and revised by Milton K. Meyers, M. D. 1913. 8vo. 564 pages. P. Blakiston's Son & Co., Philadelphia.

Appendicitis. Its History, Anatomy, Clinical Aetiology, Pathology, Symptomatology, Diagnosis, Prognosis, Treatment, Technic of Operation, Complications and Sequels. By John B. Deaver, M. D., Sc. D., LL. D. Fourth edition, thoroughly revised. Containing 14 illustrations. 1913. 8vo. 379 pages. P. Blakiston's Son & Co., Philadelphia.

Flatulence and Shock. By F. G. Crookshank, M. D., M. R. C. P., Lond. 1913. 8vo. 47 pages. Paul B. Hoeber, New York.

The Modern Treatment of Nervous and Mental Diseases. By American and British authors. Edited by William A. White, M. D., and Smith Ely Jelliffe, A. M., M. D., Ph. D. Volume I. 1913. 8vo. 867 pages. Lea & Febiger, Philadelphia and New York.

A Manual of Surgical Treatment. By Sir W. Watson Cheyne, Bart., C. B., D. Sc., LL. D., F. R. C. S., F. R. S., and F. F. Burghard, M. S. (Lond.), F. R. C. S. New edition, entirely revised and largely rewritten with the assistance of T. P. Legg, M. S. (Lond.), F. R. C. S., and Arthur Edmunds, M. S. (Lond.), F. R. C. S. In five volumes. Vol. IV. *The Treatment of the Surgical Affections of the Jaws, Tongue and Alimentary Canal.* 1913. 8vo. 622 pages. Lea & Febiger, Philadelphia and New York.

Medical and Surgical Report of the Presbyterian Hospital in the City of New York. Volume IX, July, 1912. Edited by John S. Thacher, M. D., and George Woolsey, M. D. 1912. 8vo. 622 pages. Corlies Macy & Company, Inc., New York.

The Catarrhal and Suppurative Diseases of the Accessory Sinuses of the Nose. By Ross Hall Skillern, M. D. [1913.] 8vo. 389 pages. J. B. Lippincott Company, Philadelphia and London.

New and Non-official Remedies, 1913. Containing Descriptions of the Articles which have been Accepted by the Council on Pharmacy and Chemistry of the American Medical Association, prior to Jan. 1, 1913. 12mo. 320 pages. American Medical Association, Chicago.

An International System of Ophthalmic Practice. Edited by Walter L. Pyle, A. M., M. D., Philadelphia. *Ophthalmic Semiology and Diagnosis.* By Charles H. Beard, M. D. With 13 colored plates and 71 figures in the text. 1913. 8vo. 400 pages. P. Blakiston's Son & Co., Philadelphia.

The Operating Room and the Patient. A Manual of Pre- and Post-Operative Treatment. By Russell S. Fowler, M. D. Third edition, rewritten and enlarged. 1913. 8vo. 611 pages. W. B. Saunders Company, Philadelphia and London.

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